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TWO CONDITIONS SIMULATING ECTOPIC GESTATION.[1]

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Our constantly extending knowledge of ectopic gestation leads us to believe that most cases of pelvic hæmatocele are the result of this condition. That this is not invariably the case has been shown, and at times conditions other than hæmatocele may simulate ectopic gestation. These remarks are suggested by the following cases:

Case I.—Mrs. ——, aged twenty-nine years; good family history; married ten years. Had one miscarriage followed by sepsis, a child at term, a second miscarriage at six months, and a child at term, then five years old. Had always menstruated regularly. Was seen in January, 1900, and at the time when she should have menstruated was exposed to cold and wet, with wet feet, followed by attacks of pain over the left ovary and abdomen, extending to the right upper portion of the abdomen. She made a gradual recovery. At this time there was no shock or evidence of depression from hemorrhage. The day before the patient was seen she had severe pain in the abdomen, for which morphine was given. Her husband, a physician, introduced a sound into the uterus, finding it four inches in length. But little oozing followed the introduction of the sound.

On examination there was tenderness over the left ovary and on the right side over the appendix. The abdomen was soft, not distended. On vaginal examination the cervix was small and long, not softened, and no tumor and exudate could be found. There was no sign of pregnancy. This patient remained in bed for a short time, menstruated after a slight delay, and was seen but a few times. She apparently recovered from the condition present.

Three months after this attack intra-uterine applications were made for some supposed disease of the pelvic viscera. The sphincter of the bowel was stretched to relieve irritation in that region. There was a

[1] Read before the American Gynecological Society, May 27, 1902.

vague history of intermittent attacks of pain at irregular intervals. She was seen the second time nine months after the first visit. She had just recovered from a normal menstrual period. She complained of pain over the left ovary, and this pain, paroxysmal in character, had been treated by hypodermic injections of morphine. Her pulse and temperature were normal. There was vague and indefinite tenderness over the abdomen, which was not rigid or distended. On vaginal examination the womb was almost fixed by a mass of soft material in the pelvis which gave no distinct fluctuation. The size, contour, and consistence of the uterus could not be accurately appreciated because of this mass. There were no symptoms of pregnancy, and the menstruation which had just ended had been typical. The pelvic tumor became softer, and finally gave obscure fluctuation. The pulse and temperature remained almost normal. After the patient had been under observation for some time a request was made to perform abdominal section. This was positively declined, and I left the case. A week afterward I was informed that the patient was at a hospital, awaiting my pleasure. Abdominal section was still declined, but vaginal section was permitted. The general condition had remained about the same.

On incising the posterior cul-de-sac, blood which had been clotted for some time emerged, and the finger passed into a large clot, apparently well shut off from surrounding tissue. The incision was enlarged as much as possible, the clot washed out, and the cavity packed with iodoform gauze. The patient reacted well from the operation, and at the usual time had a discharge, resembling menstruation, from the uterus. The gauze was gradually removed, and ten days after the operation all had been taken away. The patient gradually developed symptoms of septic infection, and was seen in consultation, abdominal section urged, but positively declined. She died with symptoms of acute peritoneal infection, and autopsy was refused. The material obtained after incision of the vagina was examined in the Pathological Laboratories of the Jefferson Medical College, and found to be blood clot. No evidence of decidua or embryonal tissue was present.

During my acquaintance with this case it was at no time possible to obtain from either husband or wife, or both, an accurate and coherent history of the patient's illness. It was impossible to tell how frequently the husband had made intra-uterine applications, or upon what indications this had been done. The husband is an anatomist, and the character of his work would make it difficult for him to remain aseptic.

Experience has shown that irritation of the pelvic peritoneum from various causes may be followed by the formation of hæmatocele. Kober[1] has recently reported two cases of retro-uterine hæmatocele in which a diagnosis of ruptured ectopic gestation was made, and in which abdominal section proved the absence of this condition. The first was that of a multipara, who, after violent interference with the pelvic organs, was taken with pain, hemorrhage, and prostration. Upon examination a semi-elastic tumor was found in Douglas' cul-de-sac,

[1] Centralblatt f. Gynäkologie, 1901, No. 39.

characteristic of ruptured ectopic gestation. Upon abdominal section the tubes and ovaries were normal, nor was there any pathological condition in the abdominal or pelvic organs. The posterior cul-de-sac was filled with blood clot, which was readily removed. The peritoneum was pale, and the uterine substance more friable than normal. A small portion of the uterus was excised for microscopic examination, but no abnormality was discovered. The patient made a good recovery.

His second case was that of a multipara, who, after a hard day's work, was taken with pain, sensitiveness in the abdomen, and the gradual development of weakness. An elastic tumor gradually developed behind the uterus. Upon abdominal section the left Fallopian tube was removed, as it contained a tumor the size of a hen's egg. The entire tube was removed by a V-shaped incision into the body of the uterus. The right tube showed its abdominal end entirely obliterated and the lumen of the tube filled with an odorless pus. There were several small abscesses in the right ovary. This was also removed.

The gross examination of the specimens indicated very strongly an ectopic gestation of the left tube. Upon microscopic examination, however, not a trace of evidence pointing to pregnancy could be discovered. The tumor contained serum, and had nothing to do with the pregnant condition.

In both cases the formation of the hæmatocele occurred just before menstruation, when the condition of congestion usual at this time was present. Both cases seemed to have resulted from mechanical violence, followed by the extravasation of blood from tissues altered by anæmia or previous inflammation. Experience shows that hemorrhage may occur from pelvic tissues altered by disease without the occurrence of ectopic gestation.

In this connection the possible presence of hæmatoma of the abdominal wall in pregnant women must not be forgotten. Stoeckel[1] reports two cases, and Sänger[2] reports one case in which collections of blood formed in the abdominal wall during the pregnant condition. While such tumors would not obscure vaginal examination, they would interfere with the results of bimanual examination.

Case II.—Somewhat emaciated, anæmic woman, aged twenty years. Some months previously she had an abortion between three and four months, accompanied by very profuse bleeding, which was controlled with great difficulty. She recuperated slowly for three months, and then her general condition and nutrition began to fail. She had not menstruated for several months, and showed signs of pregnancy. Two weeks before she was seen she had intermittent hemorrhages from the womb, with attacks of abdominal pain.

On examination the patient was exceedingly pale, her pulse 120 to

[1] Centralblatt f. Gynäkologie, 1901, No. 10. [2] Ibid., 1897, No. 16.

144; and upon vaginal examination the cervix was small, not much softened or shortened, and the pelvis was filled with a soft, boggy tumor, completely occupying the posterior cul-de-sac. The body of the womb could not be distinctly outlined, but was somewhat enlarged. A discharge of dark fluid blood was coming from the vagina. The breasts gave the characteristic signs of early gestation. The most probable explanation of the patient's condition seemed to be ruptured tubal ectopic gestation. Her profound anæmia and rapid pulse urged the necessity for complete diagnosis and control of the condition.

She was immediately transferred to the Jefferson Maternity and abdominal section performed. Upon opening the abdomen the tubes and ovaries were found to be normal. The uterus was completely retroverted, very soft in consistence, resembling a cyst, and filled the posterior cul-de-sac. There was no evidence of exudate or adhesion about the uterus, and it was raised to its normal position without much difficulty. The abdomen was closed, and the patient received intravenous saline infusion. The vagina was tamponed with gauze, raising the uterus and carrying the cervix backward. The pregnancy continued, and the patient speedily improved in condition until she became well enough to go to her home. She had felt fœtal movements, and the uterus had grown larger and harder.

Soon after leaving the Maternity she returned with uterine pains, and was delivered of a six months' fœtus, which moved but did not breathe. Upon examining the uterus it was found to be completely lined with a mass of clotted blood which required a blunt curette for its removal. This patient made a somewhat tedious recovery, retarded by pain in the left sciatic nerve, for which no anatomical cause could be found in the pelvis.

Shortly after the case just described came under my observation a second was seen in consultation, upon which section was done and the same condition found to be present. In this case there was more resistance and pain, suggesting pelvic peritonitis, than in the first, and the anatomical conditions found by vaginal examination were typical of ectopic gestation.

In the recent literature of the subject Ségond[1] reports the case of a patient who had borne one living child and had suffered from metritis. A diagnosis of ruptured ectopic gestation was made from combined examination, and the patient was operated upon. The uterus was found in early pregnancy, retroflexed, and partially fixed upon the left side of the pelvis. It was brought into normal position and the abdomen closed. The patient recovered from the operation and left the hospital, but aborted at six months. Routier[2] reports a case in which a retroflexed uterus adherent upon the left side of the pelvis was thought to be an ectopic gestation. The uterus was replaced after abdominal section, but abortion followed the operation.

That a retroflexed pregnant uterus may simulate other pelvic tumors

[1] Compt. Rend. de la Soc. de Obstét., de Gynecologie et de Pædiatrie de Paris, 1900, vol. ii.
[2] Ibid., 1901, vol. iii.

receives illustration in Varnier's case.[1] He opened the abdomen to remove an ovarian cyst, finding, instead, a retroflexed pregnant womb. The patient went to full term, and was delivered of a living child. Boldt[2] reported at a recent meeting of the New York Obstetrical Society a case of gonorrhœal pyosalpinx simulating tubal pregnancy. These examples from the recent literature of the subject illustrate the fact that these cases are not exceedingly rare.

The diagnosis of ectopic gestation is a subject of constant interest, and one which at times presents considerable difficulty. Aside from the anatomical features of the diagnosis, Weindler,[3] Veit, Martin, Olshausen, and others have drawn attention to the relation between the occurrence of rupture in ectopic gestation and the character of the menstruation shown by the patient. A further study of the subject from this standpoint may assist us in diagnosis.

A positive diagnosis can in almost all cases be immediately made by abdominal section. So grave a condition justifies, we believe, abdominal section, if this be necessary for accurate diagnosis. Even if the enlarged tube when removed does not prove to be the site of an ectopic gestation, the patient has suffered in no way from the operation. In cases of retroflexion and retroversion of the pregnant womb simulating ectopic gestation, abdominal section and the replacement of the womb are safer from all standpoints than the continuation of the condition. In good hands pregnancy is prolonged and hemorrhage and septic infection are prevented.

A RAPID REACTION FOR BENCE-JONES ALBUMOSE.

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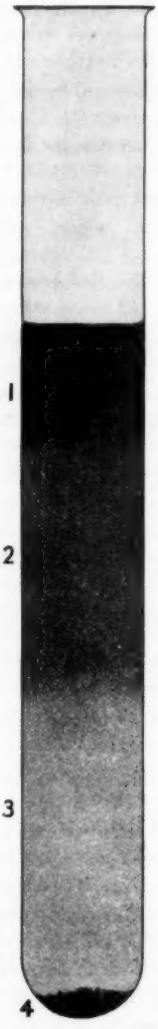
During the past two years the writer has found opportunity to employ repeatedly the various tests now in use for the recognition of Bence-Jones albumose when present in the urine. A detailed account of these reactions will not be given, and let it suffice to say that the vast majority of them are caused by the presence of other of the albumoses, as peptone, histon, and globin. Indeed, but few of these tests distinguish clearly between peptones and Bence-Jones albumose; and these differences are commonly but a variation, in intensity or degree, of one and the same reaction.

The reaction which is probably most reliable is that with lead acetate and caustic soda for the detection of sulphur. Many chemists regard the presence of loosely combined sulphur as a pre-eminent feature

[1] Compt. Rend. de la Soc. de Obstét., de Gynecologie et de Pædiatrie de Paris, 1900, vol. ii.
[2] American Journal of Obstetrics, April, 1902. [3] Archiv f. Gynäk., 1900, Bd. lxi., Heft 3.



which distinguishes Bence-Jones' albumose from other albumoses. The methods suggested by the different writers for the application of this test, while practical, necessitate considerable time for execution. The following described method has proven to be of value in economizing both time and labor; and the reactions obtained by it were equally decisive with those displayed by the more complicated methods when used as controls:

METHOD FOR APPLICATION. 1. Fifteen to twenty c.c. of the filtered urine are placed in a test-tube, and to it an equal quantity of a saturated solution of sodium chloride is added, and the tube shaken to effect a perfect mixture.

2. Two or three c.c. of a 30 per cent. solution of caustic soda are now added, shaking vigorously.

3. The upper one-fourth of this column of liquid is gradually heated over the flame of a Bunsen burner to the boiling point, when a solution of lead acetate (10 per cent.) is added, drop by drop, boiling the upper previously heated stratum of liquid after each additional drop.

4. When the drop of lead solution comes in contact with the liquid a copious pearly or creamy cloud appears at the surface, which becomes less dense as the boiling point is neared; and when ebullition is prolonged for from one-half minute to one minute the upper stratum shows a slight browning, which deepens to that of a dull black, as shown by the accompanying illustration (1).

The lower portion of the heated liquid displays less marked blacking, and below this point for some distance there is seen a variable degree of browning (2). Standing intensifies the reaction; but if this be prolonged for several hours the black precipitate falls through the clear stratum of liquid (3), collecting as a coarsely granular pigment in the bottom of the tube (4).

This reaction has been studied in the urine of a case of myeloma—dilution, one part in ten; and often a much higher dilution gave positive results. It depends upon the presence of loosely combined sulphur—a constituent of Bence-Jones albumose—which when treated as above outlined causes the lead to be precipitated in the form of lead sulphide. Phosphates when present in excess may cause a slight, flocculent, brown precipitate upon addition of the soda solution; but this browning is not of sufficient intensity to be mistaken for that of albumose.

A CASE OF ADIPOSIS DOLOROSA (DERCUM'S DISEASE).[1]

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As Professor Dercum has stated in a recent paper, only twenty-five cases of adiposis dolorosa have been placed on record. I have no doubt myself that the disease occurs much more frequently than this number would lead us to believe. The limited number of cases reported is due to the fact that the general practitioner, and even neurologists, frequently fail to recognize it. The case that I have the pleasure of reporting this evening, though not as marked as others that I have seen, is, I believe, sufficiently characteristic to merit attention.

The case is that of Eleanor G., aged fifty-six years; white; married; housekeeper; American by birth.

Family History. Both parents dead—father of unknown cause, mother of heart disease. Had two brothers; both dead—one in infancy, the other at sixty-five years, of apoplexy; also had four sisters—three died in infancy, the other living and in good health.

Personal History. At the age of twelve years had scarlatina, and made a good recovery. Was married at the age of nineteen years, at which time she weighed less than one hundred pounds. Had eight children, five of whom are living. One child is an inmate of the Home for Feeble-minded Children, at Elwyn. Two died in infancy—one of cholera infantum, the other of marasmus; and the third, at three years of age, of diphtheria.

Shortly after her marriage she noticed an accumulation of fat over both hips and over the upper parts of her arms and legs. Passed through the menopause six years ago.

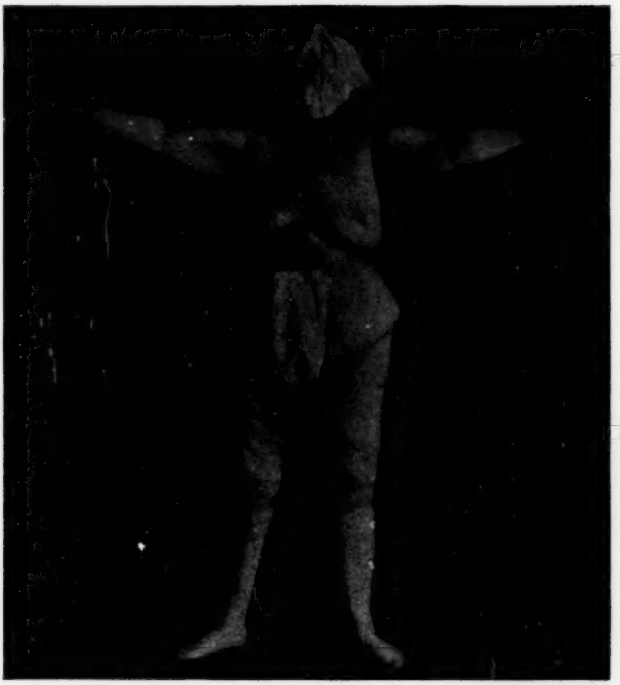
Seven or eight years ago she noticed that she became easily bruised, a blow of the slightest intensity causing pain, attended by black-and-blue discolorations. For over a year past she has suffered from sharp, shooting pains in the arms and hands. Was treated for neuritis for over a year at one of the Philadelphia clinics.

Status Præsens. On February 8th of this year (1902) she weighed 229 pounds; her present weight is 236 pounds. Complexion ruddy; has traces of arterio-sclerosis; complains of constant, sharp, shooting pains in the arms and hands. She is quickly fatigued, and presents symptoms of a neurasthenic character. There is a fatty deposit the size of an egg under the chin, which is painful to pressure. In both arms, near the axillary region, there are masses of pendulous, putty-like fat, decidedly painful to pressure. The arms below the elbows, though stout, are well rounded and proportioned. The wrists and hands are small and well formed. Pain on pressure over the back is also present. Over the hips and abdominal region the fat hangs in folds, and, as in the other regions, every slightest touch is attended with pain. The thighs, compared with the legs below the knees, are unusually large. Pressure over the fat on the inside of the thighs causes the patient to cry out with pain.

[1] Patient shown and paper read at March meeting of Philadelphia Neurological Society.

Her memory is impaired. There is no tremor of the tongue, lips, muscles of the face or hands. Pupillary reflexes are normal. The knee-jerks are plus. Romberg's symptom is absent.

The case presents the four cardinal symptoms noted by Vitaut, viz.: the enlargements, the pains, the neurasthenia, and the psychic symptoms, which here assume the form of impairment of memory and mental hebetude. The case must be classified in the group termed by Vitaut the localized diffuse form. The case is further typical in that the pains present are both spontaneous and induced. The pains are more or less constant; spontaneous exacerbations apparently do not



occur. Exacerbations are, however, provoked by pressure. The asthenia is typical in degree, ready fatigue upon exertion being very marked. The mental symptoms are also typical, though they are not pronounced. Secondary symptoms are not present. The case justifies the diagnosis of adiposis dolorosa, and is important because it presents the form with which the disease is commonly met, and which so often escapes recognition. The case before us, as we have already stated, was under observation in a public clinic for over a year without being recognized.

A FURTHER CONTRIBUTION TO OUR KNOWLEDGE OF THE HISTOLOGY OF THE GASTRIC MUCOSA IN PATHOLOGICAL CONDITIONS OF THIS ORGAN.*

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In 1896 I published a paper under a similar title.[1] For the sake of convenience I divided the pieces of gastric mucous membrane that are found in the wash-water or in the chyme according to their microscopic appearance into the following groups:

1. N.—*Normal.* Glands and interglandular tissue exist in normal proportions.

2. C.—*Connective Tissue.* While there is a normal proportion between the glands and interglandular tissue, there is a marked proliferation of connective tissue around the glands.

3. P.—*Proliferation.* There is a marked proliferation of the glands; they are nearer each other, and sometimes have an elongated and curved shape.

4. B.—*Beginning Atrophy.* The glands exist in smaller numbers and are sometimes also smaller in size, the interglandular spaces being quite large and filled partly with small-cell infiltration, partly with connective-tissue formation.

5. A.—*Atrophy.* Complete atrophy; no glands visible; only indications of their previous existence; round-cell infiltration.

6. V.—*Vacuolization.* Within the glands exist vacuoles of different shape, being the result of a mucoid degeneration of some glandular cells.

It is quite evident that this classification does not exhaust all possibilities that may be observed in pathological cases. My idea was only to furnish a foundation which may form a common basis upon which we can build further.

In my former article, to which I will again refer later, I have touched upon the older literature, and will at present cite only the more recent investigations relating to our subject.

Cohnheim,[2] in Boas' clinic, examined a large number of fresh pieces of gastric mucous membrane found in the wash-water, and came to the following conclusions: In cases of hyperacidity parenchymatous changes principally are found, consisting in a disappearance of the principal cells and proliferation of the parietal cells. In cases without hydrochloric acid the principal changes take place in the parenchyma, especially in the vestibular layer. The changes represent a mucoid degeneration of the normal cylindrical cells, and correspond to Hayem's "gastrite parenchymateuse muqueuse"—*i. e.*, the mucous catarrh of

* Read before the American Gastro-enterological Association, at Washington, D. C., May 1, 1902.

authors. In the glandular layer proper we find a disappearance of the parietal cells, with a normal amount of principal cells, as in Case XVIII., in whom the interstitial changes are only slight, and variations from the normal chemistry of the stomach are caused by these. In no case, however, is there a parenchymatous gastritis pure and simple, interstitial changes occurring everywhere to a greater or less degree, beginning with round-cell infiltration and going on to complete atrophy of the glandular layer.

In another paper,[3] dealing more with the diagnosis of cancer of the stomach, the same author arrives at the following conclusions:

1. The only absolutely conclusive sign of cancer that excludes every other doubt is the occurrence of small tumor particles found in washing out either the empty or filled stomach.

2. Nearly as pathognomic—at least according to our present experience—is the development of protozoa on the stomach mucosa.

3. The constant occurrence of pus in fetid or non-fetid stomach contents has up to now been observed only in cancer, although occasionally it may occur when a perigastric abscess breaks into the stomach, but then there is usually no mucus present.

4. All the symptoms may occur before a tumor can be palpated; they are therefore "relatively" early signs.

5. They are principally of importance in the diagnosis of carcinomata of the stomach not situated at the pylorus, since with those situated at the orifice other important signs occur earlier; occasionally, however, they are also observed in these cases.

Strauss and Myer[4] describe a case of hypersecretio continua chronica that came to autopsy. All the glands (both in the fundus and in the pylorus) can be plainly differentiated, but are coiled at their basal extremity. In some places the glands are cystically dilated. Parietal cells are increased. In the connective tissue there is round-cell infiltration, penetrating to the submucosa. In the glandular cells as well as in the gland lumen there are no leucocytes.

Martius and Lubarsch[5] give more exact numbers regarding the distribution of the glands in the stomach. They say in their book:

"I will say right here that in cross-sections of the mucous membrane of the stomach, measured just below its surface, we can see, on an average, twenty to twenty-five glands in one field (Zeiss obj. B.; Oc. 3), the number twenty corresponding about to the pyloric region, where normally the interglandular tissue is somewhat larger than in the other parts of the stomach. Corresponding with these conditions we find that the interglandular connective tissue in its broadest places has a width of five to seven rows of cells at the highest, and these places are found only directly under the surface epithelium. The nearer we approach the gland region proper the less interglandular tissue is found, consisting sometimes only of a few cells, gland lying

close to gland. If with the above-mentioned magnification the number of glands is around eighteen, and if there are found ten or more rows of cells in the connective tissue, we can with certainty speak of a proliferation of the connective tissue, even if we are unable to determine whether we have to deal with a piece from the pylorus or the fundus."

Hemmeter[6] has minutely examined the pieces of stomach mucous membrane in a large number of patients. He used my classification given above, and supplemented the same. This author says: "The objection that may be made against this is the fact that Einhorn seemingly had based his classification upon the condition of the glands and the interglandular tissue, regarding the state of the cells themselves only once in his six types. For this reason I will supplement his divisions by adding the appearance and condition of the vestibular cells and the appearance and numerical relations of the principal and parietal cells."

I would like to call attention to the fact that in these examinations we have to deal with small pieces only, where often, especially in cross-sections, it is difficult to say whether only the mouths or the deeper parts of the glands have been cut. For the same reason, numerical data relating to the principal and parietal cells would not be conclusive. Moreover, the significance of the latter has not yet been established.

The result of Hemmeter's investigation was as follows: Ten healthy persons: perfectly normal in eight; proliferation of glands in one; proliferation of connective tissue in one. Hyperacidity in twenty cases: normal in four; atrophy in two; gland proliferation in six; proliferation and hypertrophy of the parietal cells in eight. Anacidity or achylia: normal in two; gland proliferation in one; atrophy in nine.

Leuk[7] gives the following data regarding the relation between the glands and interglandular tissue in the normal human stomach:

In the fundus:

1. The number of gland openings in 1 mm. of mucous membrane (linear measure only) is about sixteen to eighteen.
2. The interfoveal connective tissue lying between two gland openings has a width of about 25 to 30 microns, measured directly under the epithelium.
3. In the middle of the mucous membrane the connective tissue between the glands has a width of 10 to 20 microns.
4. Connective tissue width in the deepest quarter of the mucous membrane, 5 to 10 microns.
5. Width of glands, 30 to 40 microns.

In the pylorus:

1. About nine, distributed regularly.
2. 25 to 30 microns.
3. 25 to 40 microns.

4. In places the same as in the fundus, but between single glands, the connective tissue may be up to 50 microns in width.

5. 45 microns.

Regarding the diagnosis of carcinoma, Leuk expresses himself as follows: "For an absolutely certain diagnosis of carcinoma from small pieces of stomach mucous membrane we must prove an atypical epithelial proliferation from the mucosa into the submucosa. Glands in the submucosa even without mitotic figures must not necessarily be the result of carcinomatous proliferation. Accessory Brunner glands in the pylorus, or simply ends of glands that have been cut off by a branch of the hypertrophic muscularis mucosæ, as I have often seen it in complete sections, might simulate a carcinoma.

"Taking it all in all, I think that our diagnostic knowledge based on the examination of chance pieces of stomach mucous membrane may be enlarged only in especially fortunate cases; in those where we intentionally try to obtain pieces for examination the condition may be somewhat more favorable."

Boekelman[8] examined pieces of stomach mucosa which he was enabled to obtain during gastro-enterostomy. He arrives at the following conclusions:

"All cases of gastric ulcer coincide in the fact that the glands lie closely together, the connective tissue being very narrow. Hyaline bodies are not ordinarily found. Many parietal cells are present, but their number is hard to estimate."

He finds:

1. The openings of the glands of normal length.
2. No goblet cells or ciliary epithelium.
3. Small diameter of the glands.
4. Little or no interstitial tissue.
5. Small round-cell infiltration in the superficial layers.
6. Few or no eosinophile polymorphonuclear leucocytes.
7. Few or no hyaline bodies.
8. Many capillaries and hemorrhages.
9. Many parietal cells, often more than normal.
10. The principal cells usually more affected than the parietal cells.

With carcinoma after ulcer the mucous membrane did not suffer much; in carcinoma without ulcer atrophy was frequently found.

The relation of atrophy to carcinoma ventriculi is described in an older paper by Rosenheim[9] in the following words:

"Atrophic processes in the stomach mucous membrane have a far-reaching influence upon the body economy. They occur more frequently than has been assumed, and not only relatively frequently with carcinoma, but also as a disease of the stomach for itself. They are without doubt important factors in the development of the so-called essential anæmia—more so than they have up to now been credited

with." "From our investigations it is evident that atrophy is the result of catarrh and inflammation, and we thus may see the most frequent and benign affection of the stomach converted into a destructive process that threatens life."

Mathieu[10] is also of a similar opinion when he says: "Interstitial gastritis with atrophy of a considerable number of glands is often met with. Not only at the border of the tumor, but also at a distance from it, the glandular elements have most often undergone a retrogressive modification which recalls that seen in gastric polyadenoma." "However that may be, interstitial gastritis and cancer go side by side or follow one another, just as in certain cases of primary cancer of the liver nodular carcinoma and cirrhosis develop simultaneously or successively."

All these authors agree with me in the main that the condition of the stomach mucous membrane in the different secretory states of the stomach is not a constant one.

FIG. 1.

Normal mucous membrane of stomach, showing relation of glands to interglandular substance. Obj. 3; Leitz eye-piece 4.

Having had the opportunity during the last six years, after the publication of my first article, to examine pieces of stomach mucous membrane in a large number of patients, it seemed to me worth while to publish the results of these more recent investigations and to enter more minutely into the details of the histological findings as well as their significance.

We have tabulated these new cases (thirty-four in all), and designated

Table of New Cases in which Small Pieces of Gastric Mucosa have been Examined, and the Result (1896–1902).

No.	Date.	Name.	Age	Diagnosis.		Gastric secretory function.		Anatomical state.	No. glands per sq. millimetre.	Remarks.
						Free HCl.	Total acidity.			
1	Feb. 22, 1896	Mr. H. C.	45	Gastritis chronica.	Euchlorhydria.	+	40	P. B.	64	Atypical glands.
2	Dec. 30, 1897	Mr. W. P.	45	Dilatatio ventric. ren mobil. dexter.		+	44	P.	44	
3	Oct. 31, 1900	Mr. C. D.	55	Gastritis chronica, hepatitis, icterus.		+	46	P. V. (?)	80	Mitoses; piece of submucosa visible.
4	Nov. 28, 1900	Mr. W. P.	44	Atonia vent., enteroptosis.		+	50	N. V.	80	Extravasations of blood; mitoses musc. mucosæ visible.
5	June 25, 1899	Mr. W. H. R.	53	Hepatitis.		+	56	P.	68	Blood extravasations; mitoses; small-cell infiltration; peptic glands.
6	Dec. 11, 1897	Mr. Alf. H.	38	Ructus, erosions.		+	56	N.	100	
7	April 4, 1898	Mr. Geo. F.	42	Erosions.	Hyperchlorhydria.	+	64	P. C.	72	Glands small in places; peptic glands.
8	Oct. 21, 1898	Mr. E. St.	27	Attacks of vomit'g, hyperchlorhydria.		+	70	C. P.	48	Large plaques of pavement epithelium.
9	Feb. 10, 1901	Mr. B. P.	36	Beginning stenosis of pylorus.		+	70	N. P. C.	88	Extravasations of red blood cells.
10	Apr. 29, 1899	Mr. M. W.	28	Dilatatio ventr., ren mob. dext.		+	72	C. P.	36	
11	Apr. 14, 1898	Miss M. W.	28	Gastroptosis, hepatoptosis, ren mob. sin.		+	72	N. C.	60	Peptic glands.
12	Feb. 3, 1896	Mr. G A. D.	32	Hyperchlorhydria.		+	76	C. P.	44	Peptic glands.
13	.....	Mr. Z.	50	Atonia vent. hyperchlorhydria.		+	80	B. C.	136	Glands small (38 microns).
14	Dec. 21. 1899	Miss A. E.	33	Gastralgia.		+	84	P. C.		
15	.....	Mrs. A.	44	Hyperchlorhydria, erosions.		+	84	C.	76	Round-cell infiltration in places.
16	Feb. 20, 1896	Mr. E. H. C.	40	Gastrosuccorrhœa contin. chron.		+	92	P. C.	128	
17	Jan. 30, 1896	Mr. W. W. S.	46	Gastrosuccorrhœa contin. chron. ulcus vent.		+	140	A.	...	No glands; fine connective tissue, probably from base of ulcer.
18	Nov. 16, 1901	Dr. D.	35	Enteritis chronica subacidity.	Hypochlorhydria.	+	26	P. V.	160	Connective tissue scanty; glands atypical.
19	Nov. 19, 1899	Dr. O. F.	42	Atonia ventric. erosions.		+	28	C. B.	52	Glands small; connective tissue rich in cells; mitoses; hyaline bodies.
20	Feb. 23, 1898	Mrs. F. L. S.	45	Dilatatio ventric.		+	28	B.	60	Glands small, indistinct; peptic glands.
21	Feb. 11, 1896	Mrs. J. S. H.	35	Erosions.		+	30	N. B.	104	Mitoses (diameter of glands 74 microns.)
22	Oct. 13, 1900	Mr. L. C.	30	Gastritis chron. erosions.		+	30	C. V. A.	48	Cell proliferation; in some cases complete atrophy; numerous capillaries; hemorrhagic infiltrations; hyaline bodies.
23	Aug. 17, 1901	Mrs. B. K.	48	Dyspepsia nervos. ventriculi.		?	?	N. C. V.	52	Some small glands; rich in cellular elements; mitoses; hyaline bodies.
24	Sept. 14, 1899	Mr. J. G. D.	40	Hyperæsthesia ventric. vomitus, achylia.	Achylia.	0	...	C.	60	Extravasations of red blood cells; glands small.
25	Jan. 14, 1897	Mrs. J. B.	60	Gastritis, enteritis, achylia.		0	...	P. A.	40	Interstitial hemorrhages.
26	Jan. 27, 1898	Miss P. P.	24	Achylia.		0	...	B. V.	120	Glands small (52 microns).
27	Jan. 10 1896	Mr. D. S.	48	Achylia.		0	...	A.	...	Some remains of glands.
28	Nov. 12, 1898	Mr. D. K.	34	Gastritis chron., splenic tumor, carc. ventr. (?)	Carcinoma ventriculi.	0 Rennet +	12	B.	40	Small round-cell carcinoma?
29	Jan. 18, 1896	Mr. M. W.	42	Carcinoma vent., ischochymia.		0	60 lactic +	C.	100	
30	Mar. 21, 1898	Mr. J. D. N.	65	Carcinoma vent. et hepatis.		+	36	C.	44	Large epithelial cells.
31	Dec. 4, 1899	Dr. W. H.	68	Carcinoma vent.		0	...	C.	...	Large spindle-shaped cells.
32	Nov. 14, 1899	Mr. M. K.	48	Carcinoma vent.		0	...	C.	20	Glands much enlarged (160 microns), filled with small round cells; epithelium of glands small; mitoses; interglandular hemorrhages.
33	Jan. 9, 1896	Mr. R. H. A.	62	Carcinoma vent., achylia.		0	...	A.	...	No glands visible, only traces of destroyed tubules can in some places be discovered.
34	Sept. 3, 1901	Mrs. P.	59	Carcinoma vent.		0	...	B.	32	Round-cell infiltration; in places more connective tissue; half-destroyed glands; hyaline bodies.

their microscopic appearance by the letters given to the various groups as described above. Before discussing the table we will first

FIG. 2.

Small glands. (Mr. Z.) Obj. 3; Leitz eye-piece 4.

FIG. 3.

Large dilated glands. (Mr. K.) Obj. 3; Leitz eye-piece 4.

consider some peculiarities of the pathological histology that we have occasionally met with, and illustrate them by means of drawings.

In order to emphasize the presence of abnormal conditions we will first illustrate the appearance of a piece of normal mucous membrane

FIG. 4.

Mitoses, one atypical. (Mrs. J. S. H.) Obj. $^1/_{12}$ oil; Leitz eye-piece 4.

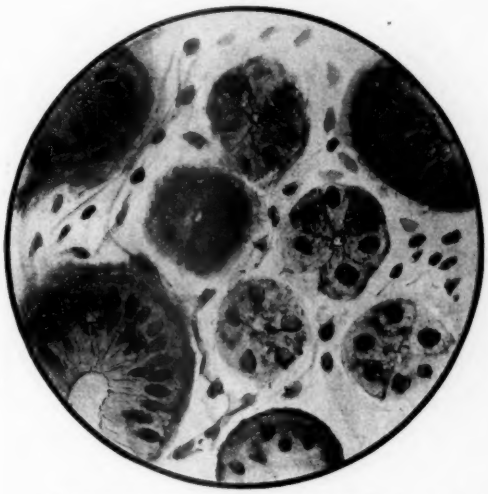
FIG. 5.

Mitoses, one atypical. (Mr. R.) Obj. $^1/_{12}$ oil; Leitz eye-piece 4.

(Fig. 1), the glands being cut transversely. This specimen was taken from the stomach of a murderer immediately after his execution, and was placed at my disposal through the kindness of Dr. R. Huebner.

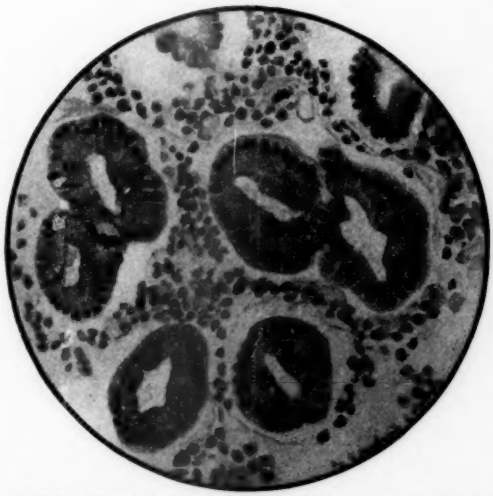
If we take the diameter of a cross-section of a normal stomach gland

FIG. 6.



Parietal cells. (Mr. R.) Obj. $^1/_{12}$ oil; Leitz eye-piece 4.

FIG. 7.



Atrophy, vacuole-like spots. (Mrs. K.) Obj. 7; Leitz eye-piece 4.

to be about 74 microns, we will find variations from this standard both above and below. Occasionally we observe exceedingly small glands, 38 microns and smaller, occurring sometimes with glands of normal size. They may be found present throughout the whole specimen. (Fig. 2.)

FIG. 8.

Fusion of glands. (Mrs. K.) Obj. 7; Leitz eye-piece 4.

FIG. 9.

Atrophy, vacuolization. (Dr. D.) Obj. 7; Leitz eye-piece 4.

On the other hand, we sometimes find especially large glands (160 microns and larger). The glandular epithelium is usually not enlarged, but there is a marked dilatation of the lumen; we would probably

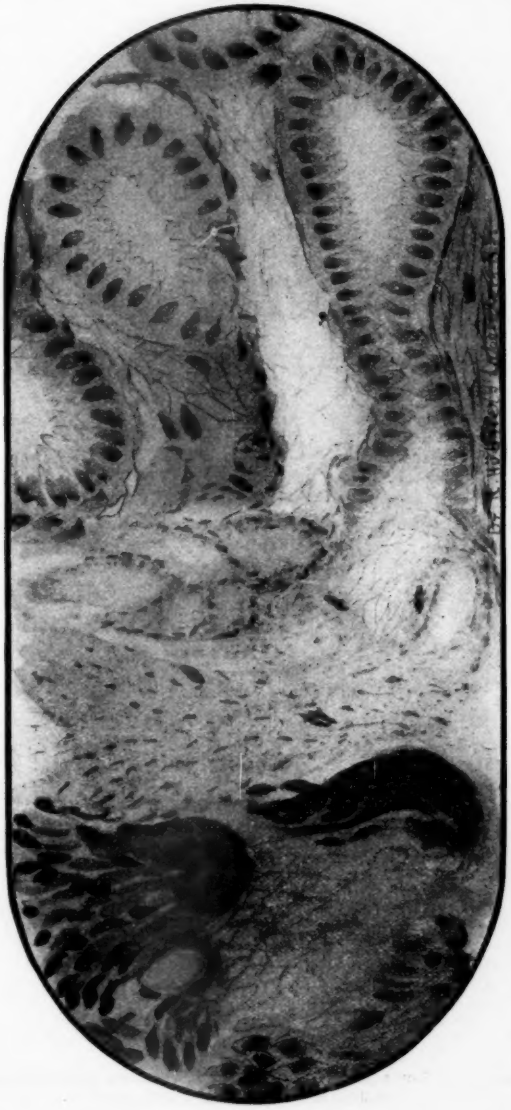


FIG. 10.

A piece of gastric mucosa, showing also submucosa and a portion of the muscular layer of the stomach. (Mr. Wm. P.) Obj. 1/18 oil; Leitz eye-piece 4.

better call them dilated glands. We have met with marked cases of this kind twice. (Fig. 3.) In most places the lumen of the gland is

FIG. 11.

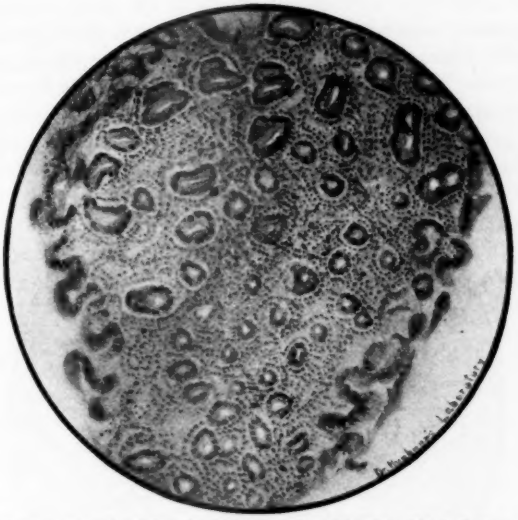
Pavement epithelium. (Mr. R.) Obj. 7; Leitz eye-piece 4.

FIG. 12.

Interglandular tissue replaced by epithelial cells, which also invade the glands. (Mr. J. D. N.) Obj. 3; Leitz eye-piece 4.

filled with cells, only occasionally the lumen being free, which may be explained by assuming that the contents have dropped out.

FIG. 13.



Atrophy; mitoses; interglandular tissue rich in cells. (Mrs. P.) Obj. 3; Leitz eye-piece 4.

FIG. 14.

Mitoses. (Mrs. P.) Obj. 7; Leitz eye-piece 4.

An infiltration of leucocytes is often observed in the interglandular structure, more rarely in the glands themselves; the latter condition may be noted in Fig. 4.

Mitoses have been observed in several of the cases; they are by no means typical of neoplasms. Figs. 4 and 5 show karyokineses in typical and atypical form, although in neither case was a neoplasm present.

An increase in the parietal cells of the glands has been observed only a few times. Fig. 6 may serve as an illustration.

FIG. 15.

Atypical glands. (Mrs. P.) Obj. 7; Leitz eye-piece 4.

In some specimens showing evidences of atrophy (increase of interglandular connective tissue, small glands, etc.) we can often observe a kind of blending of the glands, as if they were destroying one another partially. Thus we find two, three, or more glands joined to one another, parts of each gland having disappeared.

In patient K. these conditions are pronounced, and are well shown in Figs. 7 and 8. There are also present in this case vacuole-like formations in the glandular epithelium, stained light blue with hæmatoxylin and showing a fine granulation.

Atrophic conditions may be associated with real vacuolization of the glands. Both conditions are especially marked in the case of Dr. D. (Fig. 9.)

Atrophic processes may also be combined with a tortuous course of the glands and apparent increase of the glands. We find this in the case of Mrs. John B.

The pieces of gastric mucosa that are occasionally found while washing the stomach, and which form the object of our investigations, represent usually only a part of the glandular surface of the stomach. Sometimes, however, the whole mucous membrane, and in rare cases the muscularis mucosæ, or even the submucosa and pieces of the muscular layer attached, are encountered. In the case of W. P., we can plainly observe this rare condition. (Fig. 10.)

Detached shreds of pavement epithelium may be observed off and on in cases that have nothing in common with cancer. Fig. 11 represents such a condition from the specimen of patient R., with slight hyperchlorhydria.

In cases of gastric cancer we may sometimes find signs of a neoplasm in the piece of mucosa, even if the latter does not directly originate from the involved area. In the case of N., with carcinoma ventriculi, there is an extensive epithelial proliferation between the glands. Besides we may be able to demonstrate the invasion of the glands by epithelial (cancer) cells in certain parts destroying the glands. (Fig. 12.)

Patient P., also suffering from cancer of the stomach, shows the signs of atrophy, fusion of the glands (Fig. 13), numerous atypical mitoses and collections of epithelial cells between the glands (Fig. 14); also the encroachment of epithelial cells upon the glands, and, finally, atypical shape of the glands. (Fig. 15.)

(For the beautiful execution of these drawings I am indebted to Dr. R. Huebner.)

Hyaline bodies, or so-called Russell's bodies, have been found in four specimens (one case of carcinoma and three of non-malignant disease). Several of the specimens had been cut too thick, and are unsuitable for the examination of hyaline bodies, otherwise we might have found these elements more frequently. They do not seem to have any pathological significance, although they point to degenerative processes.

If we now return to a consideration of the table we find that for the various secretory states (and also organic diseases) of the stomach there is no constant condition of the mucous membrane—a fact to which we have called attention in our first article.

Even in the group of euchlorhydria (six cases) the structure of the mucosa is not always the same. A proliferation of the glands was found in three, proliferation with beginning atrophy in one, normal in one, and vacuolization in one.

In the eleven cases with hyperchlorhydria we encounter normal conditions of the gland twice; proliferation seven times, either alone or in conjunction with increase of the connective tissue; once beginning atrophy and once absolute glandular atrophy.

Five cases of hypochlorhydria without organic disease showed in one normal conditions, with beginning atrophy; proliferation, with

vacuolization, in another; beginning atrophy in two, and increase of connective tissue, with vacuolization, in one.

Four cases of achylia gastrica simplex (without organic lesion) show connective-tissue increase in one; proliferation, with atrophy, in another; beginning atrophy and vacuolization in a third, and complete atrophy in one.

Cases of carcinoma of the stomach: In one case (David K.) the diagnosis of cancer was not absolutely certain, but was very probable; in all the other six the diagnosis of carcinoma at the time of the examination was positive.

In four connective-tissue proliferation was found, in two beginning atrophy, and total atrophy in one. A growth of epithelial cells into the gland lumina was found twice.

From the varying conditions of the mucous membrane of the stomach in the same secretory anomalies we may conclude that the pathologic-anatomical state of this organ is probably not the cause of the affection. In the article above cited I have tried to apply Edinger's[11] theory for nervous diseases to affections of the stomach. I called attention to the fact that increased functional activity of an organ leads to an increased development of the apparatus kept in activity. Corresponding changes will therefore be produced in the various organs by an increase or decrease of the functional work if continued for any length of time. In the stomach with an increased secretion (hyperchlorhydria, hypersecretion) a glandular proliferation would be expected; whereas, on the other hand, in cases of diminished gastric secretion or total absence of gastric juice (hypochlorhydria, achylia, etc.) a disappearance of the glandular element would be observed.

As a matter of fact, we find this principle indicated on looking at the table. With hyperchlorhydria frequently proliferation is observed, and with hypochlorhydria or achylia frequently beginning or complete atrophy.

The reason why these changes do not always occur I have tried to explain in my former paper by the supposition that the increased or decreased functional activity had perhaps not lasted long enough to produce these changes throughout the entire organ. In addition I would like to remark that, as long as with an increase of functional activity the nutrition of the organ is good, it will hypertrophy; but if the blood supply is inadequate the organ, in spite of increased work, will show the signs of atrophy or degeneration, an exhaustion of some parts occurring, which later perish. In some parts of the stomach similar conditions may at times be present, and thus atrophic states in hyperchlorhydria may be explained.

Why do we find glands in achylia, even if the condition has been present for a long time? Each organ has a certain inherent tendency

to retain as much as possible its normal condition, even if not called upon to do much work. The glands will try to perpetuate themselves, even under the most disadvantageous conditions.

According to this explanation, extensive changes in the mucous membrane of the stomach may take place without representing any primary disease of this organ; they may be the result of functional secretory disturbances of long standing.

It is well understood that the pathological processes need not on that account always be of a slight nature, but may show the signs of grave changes.

Although from a diagnostic standpoint the microscopic examination of pieces of mucous membrane of the stomach is inferior to the examination of the gastric juice, yet it may furnish a few prognostically important points. If, for instance, marked proliferation of the glands is found, an existing hyperchlorhydria may be considered to be of a more severe character. In the same way a marked atrophy of the glands in achylia would also be considered of importance.

Martius goes perhaps a little too far when he says: "I believe that as far as the prognosis of a certain stomach trouble is concerned, the result of a histological examination would be of significance. If in a case of achylia gastrica, in spite of subjective euphoria, we should find the anatomical lesions of gastritis progressiva atrophicans, we must bear in mind that a total atrophy of the mucous membrane of the stomach, with subsequent anæmia and cachexia, will be the sad outcome."

I have seen two patients with achylia gastrica (one of whom is David S., in the above table) in whom the examination of the piece of mucous membrane showed a complete atrophy of the glands, and who, in spite of this, have enjoyed the best of health for years. Microscopic examination shows only how far the changes have taken place in the mucous membrane, but gives no hint as to the general bodily condition (how long the body may still exist, etc.). Fortunately, the human organism possesses numerous mechanisms, by means of which even grave functional disturbances with subsequent tissue changes may be compensated.

In carcinoma, also, the examination of pieces of the mucous membrane of the stomach may occasionally be of value, especially when we can demonstrate a direct invasion of the glandular tissue by epithelial cells, as this apparently seems to speak positively for carcinoma.

Footing upon the above theory that the secretory disturbances of the stomach are not dependent upon a primary disease of the mucosa, but are of a purely functional nature, caused by abnormal nerve influences, the following points would suggest themselves in the therapy of these affections:

1. Our therapeutic measures must not be directed against the stomach alone, but must take into consideration the entire bodily state. Any anomalies in the blood or nervous system must first be corrected. Everything must tend to apportion work and rest for the principal organs in an even manner, and bring them into harmony with each other. In this relation the well-known hygienic principles of a correct mode of life are of great importance.

2. Any anomalies should be corrected as far as possible. If this is not possible, everything should be done to make it easy for the anomaly, so that the organism suffers as little as possible.

As to the first point (the improvement of the general bodily condition), we must attempt to establish a correct mode of living, give tonics (iron, arsenic, strychnine, etc.) if needed, or perhaps sedatives for the nervous system (bromides, zinc valerianate, etc.). Hydrotherapeutic measures (massage, gymnastics, general electricity) and change of climate (mountains or seaside) are also of importance.

Regarding the second point (special measures directed against any anomaly of secretion that may be present), we must pay attention to a suitable diet and to direct treatment of the stomach.

In all secretory anomalies as well as in all chronic ailments the principle of giving sufficient nourishment is the main one. We must, therefore, see that the patient eats enough.

In cases of hyperchlorhydria a diet comparatively rich in proteids and poor in carbohydrates will be chosen. Albuminous substances unite with the free hydrochloric acid, thus using up some of the concentrated juice. The subjective feeling of the patient is better, and the strong acid will not so readily injure the mucous membrane of the stomach.

It has been proposed not to give any meat diet in hyperchlorhydria, as this, according to Pawlow, would tend to increase the secretion. We ought, however, not to lose sight of the fact that Pawlow's experiments, interesting as they may be, relate only to normal conditions, and cannot at once be applied to diseased states. In our cases we have to deal with persons whose stomach (probably through abnormal nerve influences) yields a very concentrated stomach juice. Here the meat diet will probably not cause an increased flow of secretion, but rather make good use of the acid, uniting readily with it on the one hand, and on the other hand being more easily digested by the excess of acid. Practically, a diet rich in proteids has stood the test of usefulness in hyperchlorhydria, and there is no reason why we should give it up.

In cases of hypochlorhydria and achylia the food ought to be rich in carbohydrates, and the amount of albumin should be decreased. A fine subdivision of the foodstuffs also is essential here. The reason for both these rules is that with the lessened secretion of the stomach

albuminous substances are digested in the stomach either not at all or only with difficulty, and in consequence mechanically irritate the bowel, causing discomfort.

Butter is not only permissible, but even indicated in all secretory anomalies.

Should there be periods of rest—*i. e.*, fluid diet—in the regimen? Although this may be resorted to for a short while, it hardly seems to be of much value, for in all these cases the primary seat of the disease is not in the stomach, and very little would be gained by special resting of the stomach. On the contrary, it seems to be more rational to regulate the diet in such a manner that it will gradually increase the work of the organs of digestion, so that the system becomes accustomed to digesting the usual foods.

The direct therapeutics of the stomach (medicaments, electricity) are generally well known, and need not be referred to here. They serve the purpose of alleviating the ailments of the stomach or to remove them.

As the result of this paper the following conclusions might be formulated:

1. The secretory functional disturbances of the stomach are not based on a primary change in the mucous membrane of the stomach. They rather produce, if they last for a longer time, lesions of the mucosa of greater or less extent.

2. The diagnosis of carcinoma of the stomach may, under specially favorable conditions, be made from a piece of gastric mucosa if a direct invasion of the gland substance by epithelial cells can be observed.

3. Therapeutically, attention must be directed principally toward the improvement of the general body state, and only secondarily by means of special measures against any secretory anomalies that may be present.

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INFECTION OF OVARIAN CYSTS DURING TYPHOID FEVER; REPORT OF TWO CASES; OPERATION; RELAPSE; RECOVERY.

By Morris J. Lewis, M.D.

and

Robert G. Le Conte, M.D.

These two cases seem to us worthy of report for the following reasons:

1. The condition is a rare one, for it of necessity implies the previous existence of an ovarian cyst in a woman suffering from typhoid fever, and the combination is, perhaps, not common. When such a cyst does exist in a typhoid case we have no means of judging how frequently it will become infected during the course of the disease, for statistics are not obtainable on this point. We have been able to collect from the literature only six similar cases, five of which were observed in Germany; but if we remember that the recognition and cultivation of the typhoid bacillus has been possible only during the last ten or twelve years, the apparent rarity of the condition is readily explained. Several cases are on record previously to 1890 where operation was undertaken for the relief of suppurating ovarian cysts, and in which an antecedent attack of typhoid fever had been noted, and it is certainly probable that some of these suppurating conditions were due to the typhoid bacillus, although the bacteriological note is wanting.

2. They are the only cases we can find in which a relapse in the fever occurred immediately following the surgical procedures. In the other recorded cases the convalescence was uneventful.

3. With the exception of Sudeck's case they are the only ones that were operated upon within a few weeks of the beginning of the typhoid fever. In the other cases three to eight months elapsed before operation was undertaken.

Case I. (Dr. Le Conte's case).—S. N., aged twenty-eight years, Russian, married, housework, admitted to the Pennsylvania Hospital September 10, 1901.

Family history negative.

Personal history negative. Has given birth to four children, one dying at the age of four months.

Present Illness. Five weeks before admission was delivered of a full-term child, and nursed it at the breast for twelve days. She was then very wretched and sick with fever, and had been confined to bed for three weeks.

On admission, temperature was 104.8° F., pulse 120, respiration 32. Color pale; tongue coated, red edges and tremulous; heart and lungs

[1] Read before the College of Physicians of Philadelphia, June 4, 1902.

negative; liver dulness extends one and a half inches beyond edge of ribs; spleen large and palpable a finger's breadth beyond edge of ribs; abdomen soft, not distended, with several rose spots, some of which look typhoidal; leucocyte count 2600; urine reddish-yellow, flocculent sediment, specific gravity 1020, acid, albumin, granular and hyaline casts; diazo reaction positive. A vaginal examination was made, as the case was admitted under the diagnosis of puerperal sepsis, but, unfortunately, the resident physician made no note of the findings. A Widal test taken the day of admission was suggestive, and two days later it proved positive. For three weeks the patient presented symptoms of a moderately severe case of typhoid fever; the delirium and stupor were at times marked, and bronchitis developed, with some dulness at base of right lung. The pulse at times was very irregular, and always weak. The temperature averaged about 101° F. to 102° F., with occasional rises to 103° F. and over, and falls to 99° F. A blood count, September 21st, showed 5450 leucocytes. During the fourth week the character of the temperature changed, and it began to assume a hectic type. At this time also the patient began to complain of pain in the pelvic region, with slight tenderness. Dr. J. A. Scott, one of the hospital staff, who had the patient in charge, called one of the writers (Le Conte) in consultation. A vaginal examination revealed a large, exquisitely tender, fluctuating mass in Douglas' cul-de-sac, which bulged in the posterior wall of the vagina and pushed the uterus up behind the pubis. The extent of the mass could not be well outlined, owing to the patient keeping the abdominal muscles rigid, but it was estimated that the cyst contained from one to two pints of pus.

The patient was transferred to the surgical wards, but for one week refused all surgical interference. Then she agreed to a simple vaginal puncture to evacuate the pus. A blood count showed 10,400 leucocytes, with 55 per cent. hæmoglobin.

Thirty-seven days after admission the patient was etherized and the abscess opened with a knife through the posterior wall of the vagina. About a quart of fetid greenish pus with many cheesy particles was evacuated. On introducing the finger through the opening, cartilage and bone were recognized in the cyst wall. The diagnosis of a suppurating teratomatous cyst was then assured. The pus removed was examined by Dr. Longcope, and showed the bacillus typhosus in large numbers and in pure culture. For the next three days the temperature for the first time went below normal, and did not go above 100.2° F. Pus was freely discharged from the vagina, and she received vaginal douches, 1:5000 bichloride of mercury. During the next week the temperature gradually rose until it reached 104.4° F. This rise was continuous and not of a hectic character, but as the discharge from the vagina was considerably less in amount, it was feared that the pus was being retained in the cyst. A drainage-tube was introduced through the vagina into the cyst, and this was flushed out twice a day with 1:10,000 bichloride solution. This, however, had no effect on the temperature, which continued to rise. The leucocytes at this time numbered 5500, and the Widal reaction was positive.

The spleen, which had retracted behind the ribs, again became palpable, and rose spots appeared upon the abdomen. A diagnosis of relapse in typhoid fever was made, and the patient again removed to the medical wards under Dr. Scott's care.

During this relapse the patient was very ill, the temperature reaching 106.4° F., and the pulse frequently being 140 to 160 and very weak. Twenty-seven days after the evacuation of the cyst the temperature reached normal, and soon thereafter became subnormal for the most part. Convalescence was uninterrupted, but a moderate discharge from the cyst continued. She left the hospital fifty-two days after operation, refusing further surgical interference, but promising to return in a few weeks for the removal of the teratomatous cyst.

Readmitted to the hospital March 12, 1902. Vaginal examination showed that the left ovary was the seat of the disease, and that the tumor was about the size of a small orange. It still occupied a position behind the uterus. March 14, 1902, ether was administered, and the cyst, together with the left tube, was easily removed through a median abdominal incision. It was lightly but universally adherent to the surrounding organs. A wick of iodoform gauze was passed through the vaginal sinus and the abdominal incision closed without drainage. The recovery was uneventful.

The following pathological report was kindly furnished by Dr. Longcope:

Macroscopic Appearance. The specimen consists of the left ovary and Fallopian tube.

Fallopian Tube. The Fallopian tube measures about 5 cm. in length. The surface, although somewhat injected, is free from adhesions, and the fimbriated extremity is open, the fimbria being delicate. The wall is not thickened, and the mucosa is normal.

Ovary. Occupying the position of the ovary is a mass the size of a lemon, which measures approximately 6 cm. in diameter. The surface is infected and contains adhesions. The mass is irregularly lobulated and feels as though composed of hard cartilaginous portions, varying with soft cystic areas.

On section, the tumor appears as a cyst containing grumous, foul-smelling pus, and its cavity is almost completely filled with irregular growths and projections from the walls. The walls, excluding the outgrowths, are about ½ cm. in thickness and covered with a reddish, velvety membrane. The largest outgrowth is about the size of a walnut. It is hard, and appears to contain cartilage and bone. Its surface is irregular and presents small, velvety cauliflower excrescences, which are sprinkled with minute yellow calcareous plates. Often smaller outgrowths project from the wall, being, in general, similar to the larger one. On section of these masses they are found to be composed of bone, cartilage, fat, and glandular spaces, all of which tissues are mixed indiscriminately together. The bony areas are, however, usually confined to the superficial portions.

Microscopic Appearance. Sections are made through different portions of the cyst wall, and the wall is found to contain many varieties of tissue. The cyst is lined by stratified squamous epithelium, with exaggerated papilla formation. No pigment is present, and the horny layer present in skin is likewise absent. Below the epithelium is a fairly dense connective tissue representing the corium. Many sebaceous glands are seen immediately below the epithelium, some of them opening through ducts upon the surface. No hair follicles are found. The

greater portion of the corium presents a marked round-cell infiltration. In the deeper portions of the wall, which is composed of a loose connective-tissue framework, several large areas of cartilage are found. In these there can be seen irregular masses, taking a deep eosin stain and containing a few contracted nuclei, evidently areas of beginning bone-formation. Small ducts and cysts are also met with, being lined by a single layer of high columnar ciliated epithelium. Their lumina contain an irregular stringy substance, which stains blue in hæmatoxylin. In one area they are very numerous, widely dilated, with low cuboidal epithelium, and give the appearance of a multilocular cyst. They are filled with a homogeneous yellow substance. The area is bordered on two sides by cartilage. In other sections masses of cartilage appear surrounded by ducts and glands, and in one place a large tubule lined with high columnar epithelium cells, with cartilage just below it, closely resembles a bronchus. In some sections the wall is filled with small round cells, lying between greatly congested vessels, and in others fat is present in large amounts. Frequently long bundles of spindle cells, which cross and interlace, are seen, suggesting smooth muscle. Occasionally an irregular mass of bone is present, or a large striated homogeneous mass, taking a deep eosin stain, probably calcified material. Surrounding the vessels are many cells of an epithelial type. In one section a large cyst is found, lined by several layers of columnar epithelium, and filled with granular material and red blood corpuscles. The Fallopian tube is perfectly normal, there are no adhesions about its surface, and the walls are thin and the mucosa is delicate.

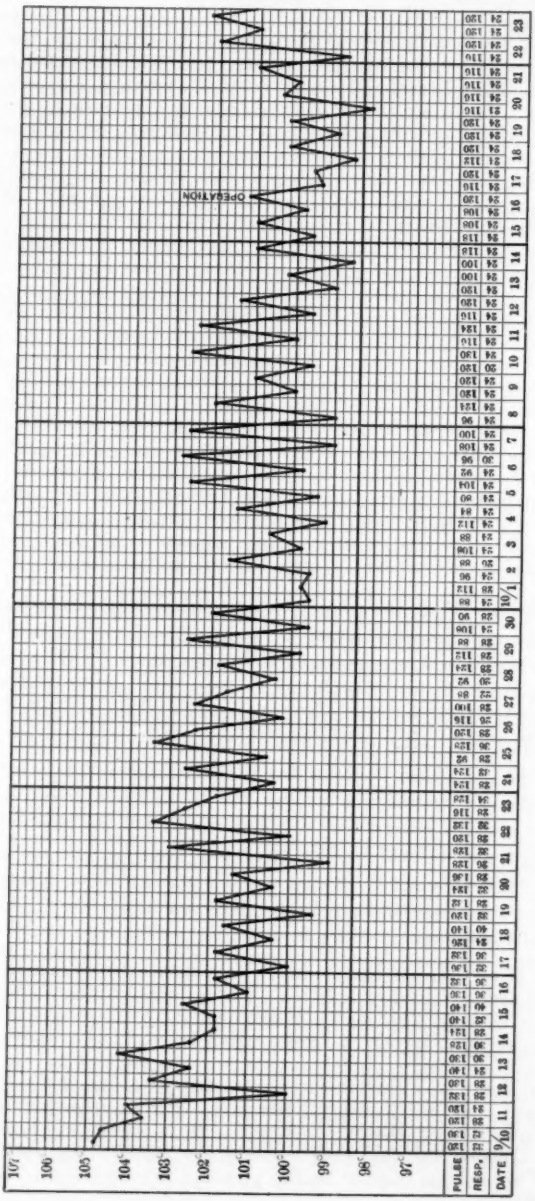
Diagnosis. Teratoma of ovary; Fallopian tube of same side normal.

Perhaps the most interesting clinical features in this case are: 1. The question of diagnosis between puerperal sepsis and typhoid fever at the time the patient was admitted to the hospital. 2. When convalescence should have been established the fever did not touch normal, but assumed a hectic character, with coincident abdominal pain and enlargement. The leucocytes, which had previously been subnormal, doubled in number. 3. After the pus was evacuated the question of whether the steadily rising temperature was due to retained pus or a relapse. This was positively cleared up in a few days, when the leucocytes again returned to a subnormal number, the spleen again became palpable after having returned to a normal size, and the appearance of a new crop of rose spots. 4. To what should the relapse be attributed? This will be discussed further on.

Case II. (Dr. Lewis' case).—Mrs. ——, aged thirty years, family and previous personal history negative. Patient was married in September, 1900, and in May, 1901, had a miscarriage in the third month of gestation, apparently caused by overexertion in packing trunks, etc., preparatory to moving.

Curettement was performed, under ether, by Dr. B. C. Hirst, and the patient made an uneventful recovery. An examination made one month later showed the pelvic organs to be in a perfectly healthy condition. During the following summer the patient was said to be not quite in her normal state of health, although she menstruated regularly,

CHART I.


OPERATION
107
106
105
104
103
102
101
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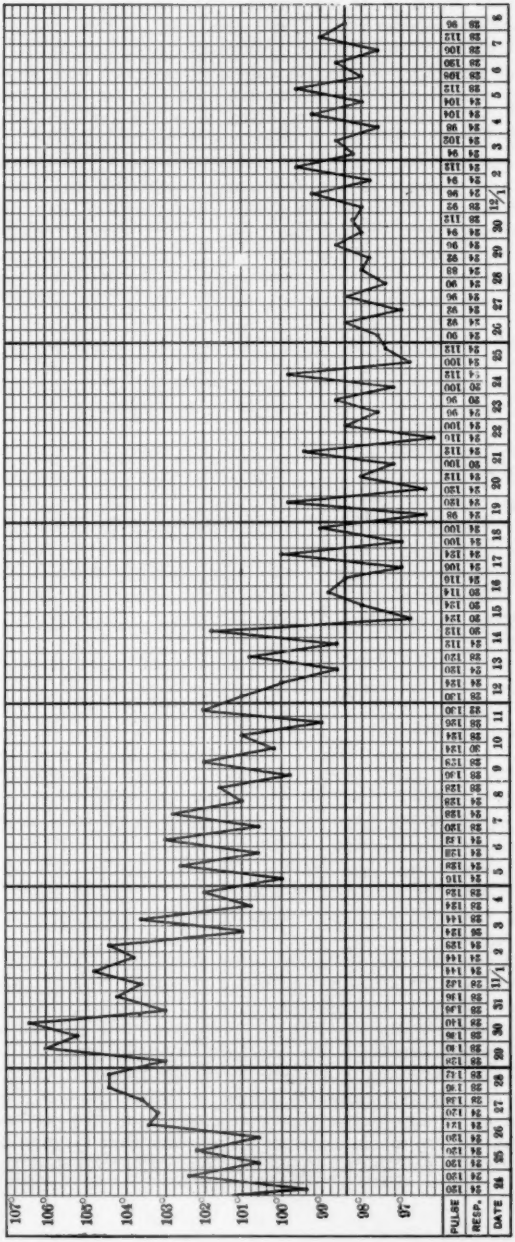
99
98
97
PULSE
RESP.
DATE

CHART I. (Continued.)



and considered herself well. On December 1, 1901, she contracted typhoid fever while in Philadelphia. The temperature by the end of the first week registered 104° F. and over, and the case assumed all the aspects of typical typhoid fever. Spots appeared, and Widal reaction was prompt and positive, and the spleen was slightly enlarged.

Nothing unusual occurred during the course of the fever, except that it was of long duration. For eighteen days the average temperature was about 103° F., after which there was a gradual decline until January 5th was reached, a period of thirty-six days. The treatment was sponging and ice-bags to the abdomen; β-naphthol was administered during the whole course of the disease, and whiskey, strychnine, and digitalis were given as seemed called for. The bowel movements, which for the earlier portion of the attack were typical in character, now began to be formed and normal in appearance, but the patient was far from well; she was occasionally slightly delirious and had persistent mild delusions. On the thirty-seventh day, when it was hoped that the patient was entering upon convalescence, the temperature rose to 102.2° F. in the evening, to fall to 97.4° F. by the next morning. There was no chill, and, with the exception of slight nausea, the patient felt fairly comfortable. Examination of the abdomen was absolutely negative.

During the next two days the temperature oscillated greatly, falling as low as 97.6° F., and rising once to 103.6° F. No chills accompanied this, and no true sweating, although there was rather free perspiration. Dr. Robert N. Willson's report of the examination of the blood on January 9th, the fortieth day, is as follows: "Blood flows easily and is of good color. Hæmoglobin, 95 per cent. Coagulability normal. Red corpuscles, 4,962,000; white corpuscles, 7800. No malarial plasmodia. No pigmented leucocytes. No poikilocytosis." No differential count was made.

On the seventh day of the supposed relapse one doubtful spot was seen, and by this time the temperature range averaged over 103° F. She began to complain of pain in the legs, and by the tenth day had for the first time a decidedly chilly sensation. No cause for this condition could be detected. There was neither cardiac nor pulmonary complication, nor could careful search determine any spot of tenderness in the abdomen, although the latter was somewhat tympanitic. An examination of the urine showed specific gravity 1009, acid, amber, turbid, sediment abundant, white, flocculent, albumin none, sugar none, urea 0.972 gm. per 100 c.c. Microscopically, full of bacteria in active motion (typical motion and shape of typhoid bacilli), full of leucocytes, very few scattered renal cells, no casts, no crystals, few squamous cells.

By the twentieth day the temperature averaged a little over 100° F., and a second examination of the blood revealed "blood rather pale, coagulation normal, hæmoglobin 70 to 75 per cent., red corpuscles 3,832,000, white corpuscles 4800, polymorphonuclear cells 90 per cent., no evident poikilocytosis." On the next day some pain in defecation was noted and also a slight asymmetry of the abdomen, the lower portion of the left rectus apparently bulging a little. No tenderness could be elicited on palpation; no mass was noticed, and the percussion-note was tympanitic, the whole abdomen being somewhat tympanitic.

On the twenty-fourth day there was some diarrhœa and acute pain

in the epigastrium, which, however, entirely disappeared after the escape of a large amount of flatus. There was now considerable distress in the rectum. Feeling sure that some serious complication existed, a vaginal examination was made, not because the patient complained of abdominal or pelvic pain, but purely for purposes of investigation.

The examination revealed bulging in Douglas' cul-de-sac on the left side, quite sensitive to pressure. A sense of fluctuation was conveyed to the examining finger when percussion was made over the left lower quadrant of the abdomen.

A third examination of the blood revealed "blood fairly good color, coagulation normal, hæmoglobin 78 per cent. (color muddy, as of leucocytic influence), red corpuscles 4,264,000, white corpuscles 9200, polymorphonuclear cells 92 per cent., no poikilocytosis."

Dr. Richard H. Harte was called in consultation. The diagnosis of pelvic abscess was confirmed, and operation immediately urged. The patient was at once conveyed to the Pennsylvania Hospital, and in one hour after admission was etherized and the operation performed by Dr. Harte. The abdomen was opened in the median line, and immediately underlying the peritoneum a large cystic tumor appeared, which was adherent to the rectum and to the left Fallopian tube. In attempting its removal entire it ruptured and a large quantity of coffee-colored, rather grumous offensive material escaped, soiling the peritoneum. Owing to its close adhesion to the bowel all of the cyst could not be removed, although most of it was cut away, and the tube and remnant of ovary removed. The ovary and tube on the right side were normal. A small fibroid tumor on the fundus of the uterus was not removed, as the patient's condition did not warrant it. Gauze packing was introduced for drainage.

A culture was made at the time of operation, from the pus from the ovarian cyst, by Dr. Longcope, and this showed subsequently pure culture of typhoid bacilli. The patient reacted well from the operation, the temperature rose during the next twelve hours from 100.2° F., which it registered immediately before, to 103.4° F., and then gradually fell to 99° F.

On the morning of the fifth day the temperature rose to 104° F., and subsequently remained at about 102° F., and the question arose as to whether there was further trouble in the abdomen or whether it was a relapse of typhoid fever. The abdominal condition seemed to be perfectly satisfactory, and after consultation it was decided that the patient was having a relapse of typhoid fever, a decision which was verified by the subsequent progress of the case.

A blood examination made at this time revealed red corpuscles 4,320,000, white corpuscles 7900, hæmoglobin 60 per cent., polymorphonuclear cells 72 per cent. A rose spot was noted on February 11th, seven days after the secondary fever. The surgical progress of the case was uneventful. After the fourteenth day of the relapse the temperature remained normal, and the patient made a perfect recovery, and is, at the time of making this report (June 4, 1902), enjoying apparent perfect health.

The following pathological report was furnished by Dr. Longcope:

Macroscopic Appearance. The specimen consists of the left ovary and Fallopian tube. Springing from the ovary is a cyst which has

CHART II.

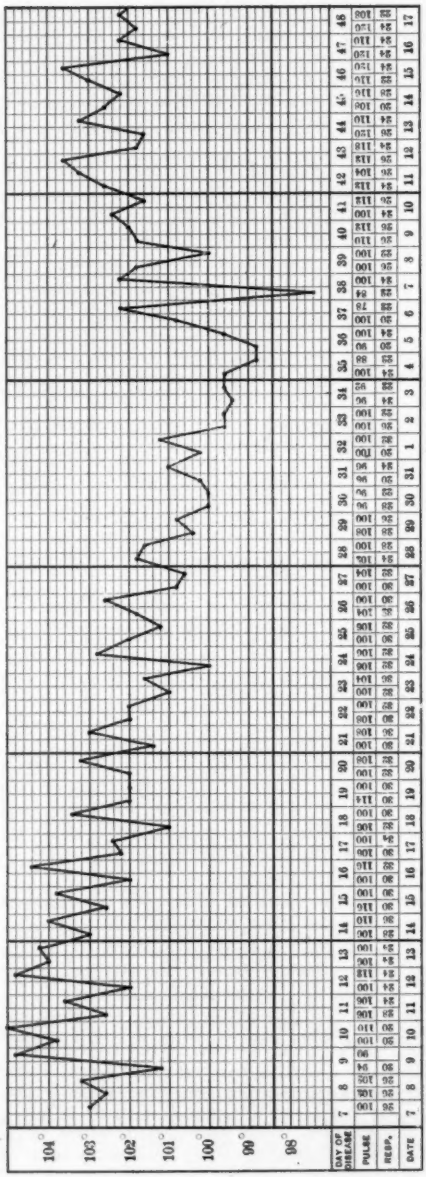
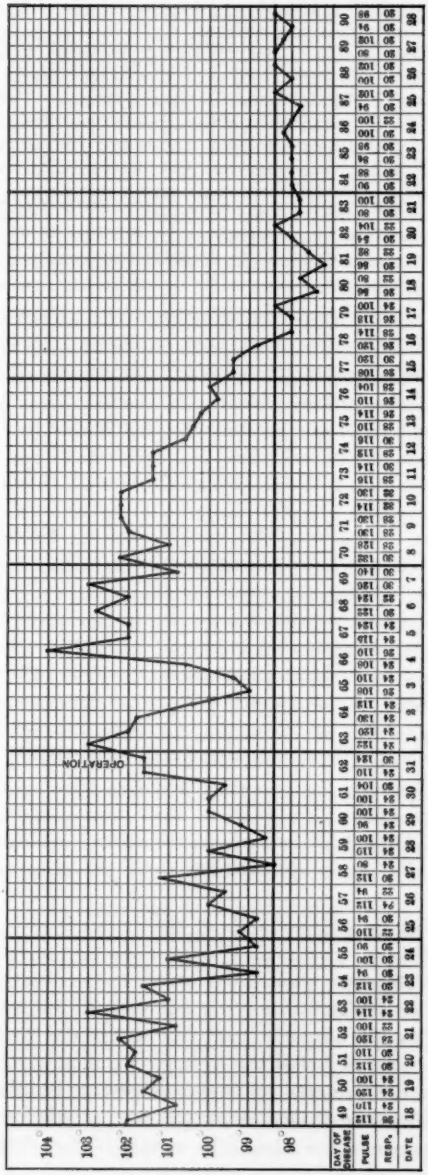

104°
103°
102°
101°
100°
99°
98°
DAY OF DISEASE
PULSE
RESP.
DATE
Dec., 1901
Jan., 1902

CHART II. (Continued.)



been opened; it apparently was the size of a small orange. The wall averages about 5 mm. in thickness and is covered by old adhesions; its inner lining consists of a soft, deeply injected tissue. The Fallopian tube is normal; its fimbriæ are delicate.

Microscopic Examination. The cortex of the ovary contains many young follicles and one large follicle. The deeper layers of the cyst wall are composed of fairly dense connective-tissue. The superficial layers consist of young granulation tissue, made up principally of large cells of an epithelial type, many of which are phagocytic. Large amounts of yellowish-brown pigment and hæmatoidin are scattered through the middle portion of the wall, and a few polymorphonuclear leucocytes are found usually in the capillaries. The Fallopian tube is normal. Cultures from the ovarian cyst give bacilli typhosus. No other organisms found. Cultures from the Fallopian tube give negative results.

That relapse should occur five days after the operation in both of these cases is interesting, and the question as to whether the operation held any causal relation to the subsequent relapses was seriously entertained. At first the question arose as to whether it was possible that the operation might have liberated the imprisoned bacilli, like the lifting of the lid of Pandora's box, and reinfected both cases, for it will be remembered that the opportunity for infection was present, in the first case through the vaginal wound, and in the second on account of the rupturing of the cyst during its removal; but further study showed this to be unlikely, and that the relationship was probably coincidental. In Werth's case the cyst, containing thin, foul pus, was ruptured and a part of its contents spilled in the peritoneum, and in Sudeck's case part of the foul pus escaped and soiled the wound, and from an abscess of the wound which occurred later typhoid bacilli and staphylococci were recovered, and yet no relapse occurred in either case. This explanation of the relapse, therefore, does not appear probable, particularly when taken in connection with the short period of time elapsing between the operation and the time of onset of the relapse, and especially as it is believed that the typhoid bacillus must gain entrance to the intestines in order to infect specifically. We are still, unfortunately, much in the dark as to the cause of relapse in typhoid fever.

The blood examinations in both of these cases is of much interest, but in neither did the findings modify the views held as to the necessity of operative interference; they served merely as corroborative evidence. In the second case the leucocyte count was 4800 on January 24th, only seven days before the operation and just before the discovery of the abscess. This count is below the average count of the leucocytes in typhoid fever, which is placed by Thayer at 5860 ("Studies in Typhoid Fever," *Johns Hopkins Hospital Bulletin*, 1901, p. 500), while the percentage of the polymorphonuclear cells was above the average of health,

viz., 90. Six days later the white corpuscles had risen to 9200, and the polymorphonuclears to 92 per cent., a relative leucocytosis. A week after the operation the leucocytes had fallen to 7900, and the polymorphonuclears to 72 per cent.

Cabot (third edition, 1898, p. 107) states in substance that in some cases in which the absolute number of leucocytes is not increased we see a relative increase in the polymorphonuclear cells, pointing to the fact that influences are at work similar to those which produce an absolute increase; and again, on p. 195, he states that this increased percentage of polymorphonuclear forms generally betrays the presence of some complication, though no increase in the total leucocyte count is present, since during typhoid fever, if uncomplicated, the polymorphonuclear forms are diminished. This case is an interesting corroboration of these statements. In the first case the leucocyte count two days after admission was 2600, and ten days later 5450. Just before operation the white cells rose to 10,400, and a few days after draining the cyst they were down again to 5500. We regret that a differential count was not made in this case.

There can be no question as to the entire recovery of the second case after the miscarriage, and the theory that the ovarian trouble could possibly date from this event is not tenable. First, as the patient was carefully examined one month after the miscarriage, and found to be in an absolutely normal condition, nor had there been any sign to indicate infection, and second, the examination of the Fallopian tube after its removal proved it to be normal, and cultures from it gave negative results. The cyst in Case II. must have existed previously to the typhoid fever, and then have become infected and grown rapidly in the short time elapsing before the operation, or it may possibly have been an infected Graafian follicle.

The six cases that have been previously reported are appended.

Case I. Werth (*Deutsche med. Wochenschr.*, 1893, No. 21, p. 489).—Woman, aged twenty-nine years; typhoid fever without complications, in October and November, 1891. In January, 1892, pain in lower abdomen began, and shortly afterward noticed swelling of the part—fever not mentioned.

Operation. June, 1892, eight months after beginning of fever. Large dermoid cyst, many adhesions and firmly bound to transverse colon. Cyst contained thin pus with foul odor. During removal the cyst ruptured and part of its contents was spilled in the peritoneum. This was sponged out, but not flushed. Recovery without relapse. Pus showed pure culture of typhoid bacillus.

Case II. Sudeck (*Münchener med. Wochenschr.*, 1896, No. 21, p. 498).—Multiparous married woman, aged thirty-two years. Seven weeks before admission to the hospital the patient had typhoid fever. Three weeks before admission noticed swelling of the lower abdomen, with pain and fever of a hectic type.

Operation. Cyst size of a ten-year-old child's head; light adhesions; fluid chocolate-colored and of a very foul odor. During the operation a small amount of fluid escaped from the cyst and soiled the wound. Abscess of the wound later developed, from which staphylococci and typhoid bacilli were recovered. From the cyst fluid pure cultures of typhoid bacilli were obtained. On section, the cyst wall showed many single and diplococci, but no bacilli.

CASE III. Pitha (*Centralbl. f. Gynäkologie*, 1897, No. 37, p. 1109).—Woman, aged twenty-five years; typhoid fever in October, 1896. Five weeks later noticed a painful swelling in right lower abdomen; no fever.

Operation. February, 1897, four months after fever. Cyst punctured through vagina. Contents, thin yellow pus, without odor. Cyst was found to be a large multilocular dermoid, and could not be thoroughly evacuated through the vagina. It was immediately removed through an abdominal incision; many strong adhesions; recovery uneventful. Cyst gave pure culture of typhoid bacillus. Sections of the cyst showed the inner wall to be necrotic in places, but no organisms were demonstrable.

CASE IV. Wallgren (*Archiv f. Gynäkologie*, 1899, Band lxix., p. 15).—Married woman, aged thirty-nine years. In 1893 patient noticed a fist-sized, movable tumor in lower abdomen, which very slowly increased in size, but never caused any particular inconvenience. During June and July, 1898, patient was in bed for six weeks with fever, but no physician was in attendance. After getting about again the tumor rapidly increased in size and became very painful. Irregular fever, with frequent chills.

Operation. September, 1898, three months after beginning of fever. Dermoid cyst containing one and a half litres of yellow-green fluid with stale odor; light adhesions, peritoneum œdematous and thickened. Recovery uneventful. Cyst fluid gave pure culture of typhoid bacillus. Sections of cyst wall also showed bacilli.

CASE V. Englemann (*Centralbl. f. Gynäkologie*, 1901, No. 23, p. 633).—Married woman, aged thirty-eight years. Typhoid fever in November, 1900; four weeks in bed; relapse in January, 1901, with great weakness, loss of flesh, vomiting, and abdominal pain. Later fever became irregular.

Operation. March, 1901, four months from beginning of fever. Dermoid cyst size of seven months' pregnancy, containing one and a half to two litres of thin yellow-green fluid; few adhesions; recovery uneventful. Cyst fluid showed a pure culture of typhoid bacillus.

CASE VI. Widal and Ravant (*Bull. et Mém. de la Soc. Méd. des Hôpitaux de Paris*, January 30, 1902, p. 45).—Married woman, aged thirty-four years. Entered hospital on the tenth day of typhoid fever. For ten days fever ran a normal course, then vomiting appeared, with a distended, tender abdomen. For four weeks these abdominal symptoms persisted, with fever, and then gradually disappeared. Fifty days after admission the temperature was normal, and the patient seemed convalescent. Three weeks later patient was out of bed, and abdominal symptoms reappeared, with fever. Abdominal section revealed a right ovarian cyst containing one and a half litres of blackish fluid. This fluid gave a pure culture of typhoid bacilli. The recovery was uneventful.

NOTE.—Since the writing of this paper there has appeared in the *American Practitioner and News* of June 1, 1902, a report by Edwin Walker, of a case of typhoid infection of an ovarian cyst. The case is briefly as follows: A young married woman, aged twenty years, contracted typhoid fever in July, 1901, the temperature rising to 103° F. and 104° F., with diarrhœa and rose-colored spots. In the fourth week pain was complained of in lower abdomen, with chills, increase of fever, and tumor. Widal reaction was present when the patient was seen by the reporter, in December, 1901. At the operation, on January 4, 1902, a large dermoid cyst was found which contained a gallon or more of pus. The cyst was firmly adherent, and ruptured during the removal, one quart of pus escaping into the peritoneum. The peritoneum was wiped out with absorbent gauze, but no irrigation of any kind was used, and the abdomen was closed without drainage. The patient recovered after mural abscesses. The pus from the cyst gave a culture of typhoid bacillus.

CLINIC OF DR. JOSEPH D. BRYANT.

1. EXCISION OF THE BREAST. 2. HÆMOPHILIA. 3. EXCISION OF THE KNEE.

REPORTED BY WILLIAM C. LUSK, M.D.,
CHIEF OF CLINIC.

CLINIC I.—*Excision of Breast.*

GENTLEMEN: I wish to-day to call your attention to the operation of excision of the breast.

The method of operative practice which we shall employ is known as the radical method of procedure, which means the removal not only of all disease manifestations that appear on gross examination to be pathologically associated with the growth, but also those tissues which one is taught to know by experience and observation are subject to cancerous infection because of their continuity with the seat of the disease.

It has been found that the tissues associated with the disease in malignant development are as follows: first, the fascia associated with the pectoralis major and minor muscles, particularly that of the former; second, almost invariably the lymphatics associated with the diseased breast. The lymphatics that suffer most frequently are those of the axillary and cervical regions; and second in frequency, especially in cases of well-developed tumors, the thoracic lymphatics of the anterior mediastinum.

It is sometimes suggested that lymphatic nodes are not to be removed except they be enlarged. I desire to say now at once and finally that

no one can say by manipulative examination only whether the lymphatics are affected or not. There is but one certain test, namely, the microscopic test, and therefore no one is justified in saying that he will not attack the axilla because he cannot determine the presence there of glandular enlargement. I have subjected to microscopic examination more than once the lymphatic glands of the axilla, so little changed that the naked eye could not determine the presence of malignancy, and found, nevertheless, pronounced malignant involvement of them. There are two reasons why the axilla should always be attacked: First, glandular involvement almost invariably exists when the patient comes under notice; second, how soon after the occurrence of malignant affection glandular involvement occurs no one can tell. It may develop slowly after infection, being of ordinary, casual progress, or it may be virulent in its type and develop rapidly. I think in this connection I may say, with eminent propriety, that the soil in which the malignant disease has its inception and development has to do very largely, indeed, with the rapidity and virulence of its action. Without operation cases of carcinoma of the breast have been estimated by Gross to live from five months to six years, or to have an average duration of life of twenty-seven months. On the other hand, when operation is practised it adds at least from a year to two years to the patient's life, and may secure immunity thereafter. Speaking generally, about 40 to 50 per cent. of those who have prompt, wide, and careful removal of the disease are exempt thereafter from any infection for three years and more. Various operators report different results. The best results obtained in the treatment of this disease amount to about 52 per cent. of recoveries after three years' time, and are reported by Dr. Halsted, of the Johns Hopkins School, based on the method of practice established by him for the removal of malignant disease, this percentage comprising those cases in which the disease not only does not recur at the seat of removal, but also does not recur in any other portion of the body. Cheyne, an eminent English surgeon, has reported 99 unselected cases, of which 56 were free from disease from one to nine years; also that in 61 of the 99, 30 were free from recurrence at the end of three years. Dr. Warren, of Boston, reports 40 per cent. of recoveries lasting three years. The rate of operative mortality is small, equalling about 2 per cent. of the cases.

The fact that I wish to impress upon you, in order to secure successful treatment for malignant disease and to increase the percentage of recoveries above that already obtained, is that certain extended educated methods of action must be insisted upon. First, the patient afflicted with a tumor must early inform someone, competent to judge of its nature, of the presence of the growth—not do, as is too often practised, hide the knowledge from everyone, and only admit the

presence of the growth when it becomes a positive affliction. Until persons afflicted with malignant disease, or having tumor manifestation, will promptly consult a physician, asking him to determine "what is the matter, and tell me what to do," we will have little, if any, better results than are now secured. Second, physicians must be so constituted that when a patient presents herself inquiring whether or not she has a tumor of the breast, they should proceed at once to make a diagnosis rather than send her away with a prescription and the injunction, "Come back again in a month or so," or "Come back again if you find it is increasing in size." That is too often the result of consultations of this character, and it is to the shame of the profession that it happens at all. One sometimes meets a class of physicians who say: "Well, it may be malignant; but in all the patients that I have had submitted to operative procedure the growths have recurred, and the sufferers have died within a year or so. If I were in your place I would not allow it to be disturbed." You may, too, in this day and age meet a stranger form of advice—one that leads patients to believe that the disease cannot and will not be cancer if they are unwilling to admit that they have a tumor at all. Another manifestation is the encouragement of quackery. My late preceptor entered a cancer hospital, conducted by a cancer quack, for the removal of a malignant growth from the lip. Now when a doctor of sense—he was a man of more than ordinary sense—willingly seeks such a channel for relief, well may it require much urging and pronounced encouragement to forestall a resort to this kind of curative effort. So as physicians you should, whenever a patient comes to you with a suspicious growth, remember that any variety of tumor is a bad tenant, because it may assume malignant characteristics; and do not ever testify to its good character until you establish its innocence by thorough examination.

Treatment. In my judgment, there is no method or practice that can compete with that effected by a free incision with a sharp knife under aseptic surroundings. If practicable, operate at once, cutting wide of the disease, removing all present disease manifestations and sites of prospective invasion. As soon as the wound heals do not send the patient away, telling her to "come back when she has further trouble." Don't do that. Advise her to see you, or some other competent physician, every month or two and undergo examination, that the first presence of any return of the disease may be promptly detected; in other words, establish strict surveillance over the possible sites of return of the growth. I have patients in mind whom I have watched for years, seeing them once a month or so, to observe whether or not any manifestation of return was apparent. If return happens promptly operate again, as wide of the seat of the disease as is prac-

ticable. Fight the disease every foot of the way, remembering not to sacrifice needlessly the patient's life and comfort for the sake of the effort of securing them. If the disease be not cured by your efforts, certainly life will be prolonged and comfort gained during the time that the affection is in abeyance. I say to you very properly that not all the surgeons indorse what I have just said; but I am consistent enough to declare that anyone failing to concur could not operate for this infliction upon me or any member of my family.

Now let us get the history of this case. The patient's age is sixty-two years, a little over the average time when cancer occurs. She is German. While I do not care to be personal in my remarks, still, in some portions of this country, particularly in Buffalo, the rate of mortality from cancer in German people, recently determined, is largely in excess of that of the native born. This fact may have a bearing on the question of the cause and the nature of malignant disease, as to whether it be due entirely to tissue change or whether it be of infectious origin. The family history of this patient is good excepting possibly that part relating to one sister who vomited blood before death. That manifestation might mean cancer of the stomach. You are not, however, to understand by any means that all cancers are hereditary; on the contrary, only about one-third. Cancers may be regarded as hereditary not in the sense that cancer *per se* is transmitted from one generation to another, but that the tendency or the vulnerability is transmitted. The habits of the patient are good. She denies all venereal disease. There is no particular association between venereal disease and cancer. The personal history does not, therefore, point significantly to anything of a causative nature in the production of malignant disease. Now notice this statement: "One year ago I first noticed a small lump in the left breast, which was not tender or painful." Tumors distinctly painful and tender at the outset are not malignant, as a rule. "This tumor was about the size of a hickory-nut, freely movable, gave rise to no inconvenience, and grew slowly. Last September I noticed a marked enlargement; still no pain unless handled, then quite tender. About that time"—please notice the nipple of the patient while giving heed to this remark—"nipple began to retract." You are not to understand that retraction of the nipple means malignancy in all instances. You are to understand that the tissue changes in the gland have caused retraction of the nipple, and that such retraction is often attendant upon malignant disease; also that malignant disease is often present in the gland without retraction of the nipple. It is one of the symptoms worth heeding, but is not diagnostic. "And the skin seemed to become grown to the tumor." Please note that the skin is adherent to it because of cancerous involvement. Integumentary adhesion is of

more pronounced importance than is retraction of the nipple, but when the two are taken together they become very significant as indications of malignant disease. Notice there is no deep adhesion of the tumor. I have examined the patient carefully on two occasions and found no enlarged glands, and Dr. Dittrich, who has kindly presented the patient for operation, also tells me he found none. Shall we, therefore, let the axilla alone or shall we invade it?

Class. Invade it.

We will invade it, and I will speak to you of the procedure as we go along. There are many operative incisions recommended, but it is important always to make the incision to fit the case. The first proposition is that the incision should be so made as to cut wide of all disease—the wider the better consistent with proper closure of the wound. I should say in this connection, for fear of being misunderstood, that in large growths closure of the wound is of no significance compared to complete removal of the disease. In such cases as these, skin-grafting and plastic sliding of the skin should be employed to close the gaps. Remember that running out from the breast, usually toward the median line, often below it, are accessory portions of the gland. Here is a marked one. Unless careful, one will leave behind the accessory portions. Let me tell you something else: It is advised to remove the breast and lymphatics together, not to cut transversely and remove the breast and then clean out the axilla, the idea being that transverse division of the lymph channels means the escape from them into and upon the tissues of the infecting cancerous agents. This is carrying the danger of infection a step further than is ordinarily considered to be necessary. We will not divide transversely any of the tissues. Please note the pectoralis major muscle. I dissect back only the portion coming from the thorax, not disturbing in this instance that coming from the clavicle, which, when not diseased, should be preserved for its functional utility. Often the cancerous deposits are found lodged in the pectoral fascia, not yet having had sufficient time to extend to the muscle. Usually their presence here can only be determined by microscopic examination, so that if on later examination disease be found in this fascia we will know we have done right in removing it, as well as the muscle lying beneath, if it, too, is affected. If we do not find disease of the tissues we will, nevertheless, not regret their removal, since this precaution can at least cause no special harm to the patient. There, under the pectoralis major, is an axillary gland, big from disease, its presence not before detected. I now push aside the pectoralis minor, raising it up so that the fascia beneath it can be well seen and removed. Gentlemen, let me point out the fact that an enlarged gland is found very frequently on the upper surface of the first rib, and you should look carefully

for it. My finger now rests on the first rib, and a brief examination enables me to feel the enlarged gland. We usually find this gland enlarged, especially when the glands lower down are invaded. Please remember, however, that this disease not infrequently omits one gland or more in its progress and becomes lodged in a gland beyond.

We will now carefully isolate the vessels. In this matter the rule is to go down at once upon and expose them, as it is a much easier and securer practice than feeling the way unguided by a view of the vessels. I am sorry to notice that the disease is very close to the vein and perhaps adherent. No, it is not adherent. What would you do if malignant disease involved the vein? Would you leave it behind or would you remove it and the diseased segment of the vein?

Class. Remove it.

Yes. Is there danger attending a fractional removal of the vein or the tying of it at this situation? Yes; gangrene. A question is sometimes raised whether it is not quite as wise to tie the artery simultaneously with the vein, so as to prevent the arm from becoming overcharged with blood, as occurs in the instance of ligaturing the vein alone. In this connection the statistics of Niebergall relating to the ligation of the femoral vessels are instructive. In 16 cases when both common femoral artery and vein were tied during operations for removal of tumors of the thigh, 62.3 per cent. developed gangrene, and in 8 cases when both were tied for trauma 50 per cent. developed gangrene. On the other hand, in 25 cases in which the common femoral vein alone was tied during removal of tumors no case developed gangrene, and in 10 cases in which the vein alone was tied for trauma but 1 case developed gangrene. This one, however, occurred in 1813, and few details were known regarding it. These figures, therefore, show the undesirability of tying the artery simultaneously with the ligature or resection of a main venous trunk. Furthermore, in support of non-ligation of the artery when the vein must be tied is the demonstration of Niebergall of the utility of the arterial pressure to overcome the resistance of the valves in restoring the circulation through the collateral venous branches. In removal of the breast it should not be forgotten in this connection that many of the collateral vessels are already destroyed by the "cleaning out of the axilla." I am now separating the final part of the growth, and will wrap around its major portion gauze, to prevent tearing the separated portion and possible infection of the axillary wall. The tumor and axillary mass are now removed entire, and I will place them on a plate, so that you can feel the glandular enlargements. We find in the mass six, including the one high up. I wish you to feel and see them, and recall the fact that here is a patient in whom enlarged glands had not been disclosed by manipulation, yet there are six extensively diseased glands, the majority

of which are of considerable size—one the size of a small walnut. Please notice the large amount of fat contained in the axilla, which did much to disguise the ability to determine the presence of the enlarged glands by manipulation. What I wish to impress upon you is that, notwithstanding our careful examination at the outset—notwithstanding the physician of the case was unable to feel enlarged glands, or the house surgeon, or Dr. Lusk, or I—they nevertheless were present. Now how absurd it is to say one should not invade the axilla because one cannot feel enlarged glands there.

I have never yet experienced disease-return in the axilla, or, perhaps, to make a more sweeping statement, disease-return in a place accessible to removal after a complete dissection like the one you have just witnessed—which means, of course, that all the lymphatic glands, vessels, fasciæ, and structures in any way directly invaded, or prospectively so, by malignancy were removed; but I have had the disease too frequently recur in the thorax, either deep in the chest or in the anterior mediastinum—in the latter locality conveyed by the lymphatics that originate in the breast and pass through the intercostal spaces near the border of the sternum. There exists an involvement of the glands in the anterior mediastinum in a very small percentage of the cases, taking them as they go. Out of 128 autopsies, Dr. Samuel Gross—who wrote the first systematic, convincing work in modern times on this form of malignant disease—records an involvement of the intercostal muscles in 1.35 per cent., of the ribs in 2.8 per cent., and of the pericardium in 2.34 per cent. of the cases. Now as regards the glands above the clavicle, Gross determined some years ago by manipulation their involvement in 6.25 per cent. of the cases. However, when you notice that in this case I was quite unable by manipulation to find the enlarged glands in the axilla, you can readily understand that the actual percentage of occurrences above the clavicle must be in excess of Dr. Gross' figures. More recently Halsted has found by careful microscopic examination of the tissues removed from above the clavicle in these cases an involvement of 34 per cent. So you have, then, the glands above the clavicle, those in the axilla, and those in the thorax itself as the common seats of involvement. It is now generally conceded on the part of all experienced surgeons that the axilla should be thoroughly cleaned out. As regards cleaning out the space above the clavicle, there is probably a wider difference in opinions on the part of operators. If enlarged glands can be felt above the clavicle, nearly all, it seems to me, practice their removal; but whether or not this region shall be exposed, and all the tissues removed when glands are not discernible, there is a difference of opinion. The majority do not clean out the tissues above the clavicle unless there be palpable evidence of disease. I have practised both

methods, and whenever I have left the space uncleaned because no evidence of enlarged glands could be determined, there has not yet been an instance in which disease has subsequently manifested itself in that situation. Glands have in several instances been removed from the anterior mediastinum, but an operation of that kind is quite impracticable. I have never attempted it, nor do I now see my way clear to make a beginning. I certainly do not yet expect to teach it because an operation of that kind, indiscriminately practised, would beget discrediting operative disaster, and by reason of the association of the disease with the pleura and other important structures within the thorax, beyond the point of any benefit from reasonable operative interference would result in no commensurable advantage.

We will now examine above the clavicle. I pass one finger into the wound up under the clavicle. I place the fingers of the other hand on the skin of the neck above, and between the fingers of the two hands I can very readily palpate a large area of the included tissues. I feel nothing suggestive of disease, and in a patient of this age I am not disposed to prolong the operation by removing these tissues with a view of excluding any supposed infection that may be present. Instead, her physician will examine her carefully at stated periods, and if any enlargements occur above the clavicle they can be promptly removed.

The wound is washed out with hot saline solution. Be very careful that all oozing points are closed. I advise making dependent drainage, and I usually do it. It should do no harm if it does no good, and though it may do no good, harm might come without it. One hears sometimes that when one drains a wound he lacks confidence in his technique. That does not follow at all. It simply means that he throws around the patient every security, recognizing the possibility which every surgeon experiences now and then, of the miscarriage of his keenest efforts to prevent the occurrence of infection and its consequences. I protest against any imputation of having lost confidence in my technique because of draining the wound. We will sew the flaps together with silkworm-gut; then so apply pressure as to exclude all possibility of dead spaces. Do not bind the arm to the side; let the arm remain loose. One argument used against the operation you have just witnessed is that it maims and mutilates the patient without producing adequate return. It is said that one cannot properly use the arm. The delayed ability to use the arm is due, more than anything else, to its being confined to the side too closely. I expect a week from to-day that the patient will show you that she can move her arm without any special trouble whatever, except possibly because of tenderness.

CLINIC II.—*Excision of Breast (concluded).*

The highest temperature of the patient whose breast I amputated a week ago is 100.4° F., and these are all rectal temperatures. The patient has had no trouble whatever; has expressed herself as being entirely comfortable, which is really somewhat unusual, and contributed to, in my judgment, largely because of the fact that the arm was not bound to the side of the body. The wound has not been dressed, as the patient has been perfectly free from annoyance, and on removal of the dressing we find that union throughout has taken place by first intention. Note that the patient has considerable abduction as well as forward motion of the arm preserved, and that she moves the extremity freely, even placing it upon the head. I wish to call your attention to two signs suggestive of return of the disease not always considered. One is tenderness of the sternum, with possible projection or thickening of the bone, and the other is tenderness of the humerus. The glands have been reported by Dr. Dunham as being extensively disorganized by the presence of cancerous growth, including the highest one—the one taken from the first rib.

I think I should say to you, in connection with the topic of surveillance of patients after an operation, that they will ask you, as they have asked me many times, "How will I know when it is coming back?" Answer them as I do, "You will know when I tell you, or when some other physician tells you, when it is coming back." Don't tell them anything specifically about it. Should you do so they would promptly imagine themselves having in succession, if not all at once, everything suggestive which you mention, much to their loss and with no gain to anyone. No. Cause them to come to your office once in a month or so, and examine them carefully at the situations which you know for manifestations of recurrence. Only in case patients are going far away, and cannot, therefore, avail themselves of a periodical careful examination, may you tell them that they might find some change in this or that part of the body as suggestive of recurrence.

HÆMOPHILIA. I wish incidentally to speak of another matter that seems to me of considerable surgical significance. There is at the present time in the hospital a patient requiring operation, but the patient objects, on the ground that he is a "bleeder." One should not always respect these statements. Patients are not always "bleeders" who pronounce themselves to be such. By way of illustration: Not many years ago a patient came into the hospital suffering from an acute attack of appendicitis, which, in my judgment, demanded a prompt operation. He objected, on the ground that he was a "bleeder," and had been warned by his physician by past experience to always make that statement to one who might purpose to

operate upon him, because he came near dying on some particular occasion in the past. I regarded that statement of course with profound respect, and declined any further to consider the question, and allowed him to pursue his course, so far as appendicitis was concerned, with simply expectant treatment. Not long thereafter an abscess pointed, and the question of opening it or of allowing it to pursue its way came up, and it occurred to me that the best plan to settle the "bleeder" question was to make a slight incision through the skin over the abscess, relying on pressure to control any tendency to undue hemorrhage. This was accordingly done, and the hemorrhage was controlled as easily as in any other patient with a more favorable history. In other words, if this patient had been a "bleeder," he had recovered from the predisposition or the causes that gave rise to it. Now the present case that we have has led me to suggest the same line of treatment—endeavor to prove whether or not the patient is correct in his assumption or opinion before acting on the proposition that undue hemorrhage will happen as the result of a necessary operation. The trial incision in this case has also shown that the blood clotted as promptly as could be wished.

EXCISION OF KNEE. The patient on whom I operate to-day is M. C., aged twenty-eight years. Family history negative; drinks moderately; denies venereal history; never sick. About eight years ago he received an injury to his left knee while playing football, from which he at first apparently recovered. However, soon afterward the leg began to flex, and we now find it ankylosed in a position at right angles with the femur. You will notice here a complete posterior displacement of the head of the tibia. This will be the twenty-fourth or twenty-fifth excision of the knee which I have practised, and of that number one only has died, she having died from sepsis, being septic at the time of the operation. One patient lost the limb as the result of the operation, due I won't say to my carelessness, but rather to my misfortune in having cut a hole in the popliteal artery while dissecting it off from the posterior ligament in the presence of badly diseased tissues. I promptly amputated the limb. This case presents the worst deformed limb I have ever had to deal with. Having applied an Esmarch bandage, I now begin with a transverse incision in front of the knee and reflect upward the flap. The idea is to excise the joint and bring the bones together in such a way as to make the limb straight. I am dividing the external hamstring tendon, taking care not to cut the external popliteal nerve. We next saw the lower end of the femur, which is the bone that should be sawn first, and the question is how to do it. First place the saw so that its cutting edge is parallel with the inferior surfaces of the condyles; second, incline the blade so that it will cut in a direction from before backward at

right angles to the long axis of the femur. To guide me in determining the correct inclination, I place along the side of the thigh a straight instrument in a direction corresponding to the long axis of the bone. Having established the proper position of the saw, I cut through the condyles. We will now saw squarely off the upper end of the tibia. It can be readily seen that the plane of section through the femur is so cut in an antero-posterior direction as to enable me to set the leg in the fully extended position, while at the same time it is so inclined transversely as to preserve the normal lateral obliquity of the tibia in its relation to the femur. How much I have to saw off I do not know. We save all we can of the ends of the bones composing the joint, saving in a young subject the epiphyseal cartilages, if possible, so that the limb may continue to grow. This man is past twenty-eight years, and therefore the epiphyseal cartilages play no part in the operation. . . . I am not heedlessly using a knife around the popliteal space—you remember the accident that happened to me a long while ago. I am hugging very closely the posterior surface of the tibia. . . . Now, having sawn both bones, let us see if we can get their surfaces together. You notice, gentlemen, we cannot bring them together suitably because of too great tension, but if they had come together readily their relations would be all right. We have got to saw off more bone. Now you might be prompted, rather than to remove any more, to bring the bones together as best you could. Let me say to you that an action of that kind would be followed almost invariably by backward displacement. They must go together pretty easily in order to avoid subsequent flexion. I remember very well my first case of excision of the knee. I met with a condition of things not as obstinate as this exhibits, but the coaptation was not suitable. I endeavored to hold the leg forcibly extended, and the result was a failure. I have now removed more from the femur, and there is still a strain on the posterior tissues; not much, however. The question is whether, when we extend the limb, we make the tissues of the leg so tense as to interfere with the circulation; that happens. I am disposed to take off a little more. . . . With the removal of this last slice the bones can be brought perfectly together. They go together firmly, not overfirmly, and hold themselves in place. Gentlemen, you see how much trouble the excision requires. Now the question arises, Shall we dress this before we take off the Esmarch bandage or not? I have on a number of occasions dressed the limb, taken off the Esmarch, put the patient to bed, and never had any significant hemorrhage whatever. On the other hand, suppose I had done so to the patient in whom I cut the popliteal vessel some years ago: What would have been the outcome then? What vessels can bleed in this case? The articular branches only. However, I will do

here the way I wish you to do, namely, remove the Esmarch before applying the dressing and attend to hemorrhage. I have removed all the pressure, and you see the hemorrhage is very slight. This is just about the amount of hemorrhage that one has in these cases; so I am warranted in saying to you that I could have closed the wound and dressed the limb immovably before relieving the constriction without any need whatever of opening it subsequently. But let me instruct you to always examine the wound. The bones need not be fastened together, because they are held firmly in place by the extended position of the leg.

Now it remains to drain posteriorly with silkworm-gut, to sew the wound with the same material, wrap around the limb aseptic gauze, so as to hold the tissues firmly in place, and put a splint upon it. The limb should be elevated to encourage return circulation. At the end of three days it is better to dress it. I should feel that one dressing was quite sufficient for this, assuming that it goes as nicely, as we hope it will.

RESULT. Primary union of the deep structures, delayed union of a limited portion of the wound because of feeble circulation, no suppuration. After three months very firm fibrous union, allowing only exceedingly slight mobility, evidently undergoing bony change.

KERATOSIS OF THE PHARYNX.[1]

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THE investigation and study of that interesting pathohistological change characterized by the formation of horny-like white tufts, occurring most frequently in and about the tonsils, in the lateral wall of the pharynx, at the base of the tongue, at the pharyngeal vault, known as mycosis pharyngea leptothricia, has, through late investigations, become a subject of great interest from an etiological and pathological point of view.

The disease under consideration is evidently not a new one, although the frequency of its discovery and the increase in the number of observed and reported cases within recent years would seem to indicate that such was the case. More exact and careful observation and greater thoroughness in differentiation is, no doubt, responsible for this increased number of reported cases. As the process of differentiation becomes more thorough, and as we add to our clinical observation, through the aid and assistance of the bacteriological and histological laboratories,

[1] Presented as candidate's thesis in the American Laryngological Society, May, 1902.

we may find that certain conditions existing in the pharynx, which on clinical examination appear to be alike, may be produced by entirely different etiological factors and give an entirely different pathological picture. Thus it may be that we have under the general term of mycosis of the pharynx been clinically including two different conditions, viz.: keratosis of the pharynx and true mycosis pharyngea leptothricia.

From the time of the presentation, by B. Fraenkels, of a case of pharyngomycosis before the Berlin Medical Society, in 1873, until the appearance of the excellent article by Siebenmann, in 1895, there appeared to be no diversity of opinion to the generally accepted theory that all forms of white spots, or tufts, occurring about the fauces, running a chronic course, without definite symptoms and evidence of local or constitutional disturbance, were due to the presence of the leptothrix buccalis, which, when searched for, was usually found in scrapings made from or adhering to the removed tufts. The investigation of the so-called mycotic disease of the pharynx can be traced from the description by B. Fraenkels and his successors, who satisfied themselves with the examination of the tufts for the existence of the parasite, in its progressive differentiation, through the work of Heryng, O. Seifert, Krieg, Colins, Garel, and Wright, who noted the pathohistological changes, as well as the presence of the leptothrix, to the more thorough study of the pathohistological changes and their relationship to the leptothrix by Siebenmann, A. Brown Kelly, F. Friedland, and D. Braden Kyle.

My object in considering this subject is for the purpose of adducing further proof to that furnished by Siebenmann, A. Brown Kelly, F. Friedland, and Kyle, that there is a condition of the pharynx which is a true keratosis, and that this condition is often described as a pharyngomycosis.

The leptothrix was first described by Leeuwenhoek in 1695. This parasite, as well as many others, invades the buccal cavity, and is usually present as a harmless guest.

The disease which we have been considering occurs in several forms, which are, no doubt, in part due to the location of the deposit and the age of the process. Thus we have minute, pin-point-like, intensely white spots, on a level with the mucous membrane, of which they seem to form a part; then the broad, plaque-like white masses, projecting above the surface of the mucous membrane, seen most frequently on the pillars and lateral walls of the pharynx; and, lastly, the conical or triangular-like horny projections from the mucous membrane, protruding from 2 to 8 mm. above its surface. This latter type is observed most frequently on the surface of the tonsil, on the surface of the lingual tonsil, and the epiglottis. These latter-described tufts, or

quills, are the most frequent and most characteristic manifest lesions of this disease. Quills so disseminated over the faucial and pharyngeal mucous surfaces, projecting out as distinctly bright white spots from the tonsils, pillars of the fauces, lingual tonsil, and the glosso-epiglottic folds, with the mucosa from which they grow showing no evidence of inflammatory activity, present a most characteristic picture. The tufts are small, tough to horny-like in hardness, firmly adherent to the mucosa, from which they can be separated only with difficulty, and when removed from the living tissue they do not undergo disintegration. One of the characteristic and peculiar features of the disease is the rapid reproduction of the tufts when forcibly removed. New tufts, on the other hand, are slow in their development. The firmest, hardest, and most elongated quills grow from the base of the tongue and the crypts of the tonsils. Those growing about the isthmus of the fauces are frequently surrounded with a soft, pultaceous substance; those found at the base of the tongue and the pharynx are usually without the addition. The most frequent seat of the presence of what is known as keratosis pharyngis is Waldeyer's lymphatic chain, although the condition is not limited solely to this region. The growth is most abundant on or about the tonsils and at the base of the tongue. Frequently the tonsil will be studded with a half dozen or more distinct tufts, while between the pillars and the tonsil and at the upper fornix will be found a continued succession of tufts, making almost a continuous white line. Over the base of the tongue they are often observed in ideal representation, which is, no doubt, due to their protection. Often we find tufts on the glosso-epiglottic folds and in the glosso-epiglottic fossæ. We have observed these, also, quite frequently on the lateral wall of the pharynx, on the epiglottis, and at the vault of the pharynx. Tufts have been observed by A. A. Gray and H. H. Curtis in the larynx. Gray states that the deposit observed by him was situated upon the left arytenoid. John Dunn, of Richmond, describes a case wherein he found the deposit on the pharyngeal tonsil, as have Garel, Strubing, Schmidt, and Labet. Jonathan Wright has observed the same condition in the nasal chamber, and Pooley has stated that he has observed this condition on the conjunctiva at the inner canthus of the eye. In Dulin's case the whole upper air tract seems to have been the seat of its invasion. Many observers state that the tufts vary in color from a white to a yellow. I wish particularly to emphasize the fact that in all of the cases in which I have observed these tufts they always had a distinctly pearly, clear white appearance. I have observed this condition most frequently in young adult life, thus agreeing with the observations made by others. I have never seen it present in a person under fifteen years nor in one over thirty-five years of age. Those in whom I have noticed this affec-

tion have been robust adults without any constitutional disorders. In several cases slight disturbance of the gastro-intestinal tract was noted, the correction of which seemed to have no influence on the local affection. Most writers state that the disorder occurs most frequently in the female sex, and such has been my observation. A. Brown Kelly places the ratio as three to one in favor of the female sex. Heredity, occupation, and hygienic surroundings seem to have no relation to the disease as producing agents. Most cases are observed in the well-to-do. It is possible that it may affect those in more moderate circumstances; but it is strange, if such be the case, that it is not more frequently discovered in dispensary and hospital practice. Climatic conditions seem to have no influence, and the season of the year to have no effect upon its prevalence. As I have already stated, the general health seems to be the most perfect in all those whom I have observed affected with this disturbance. Delavan, Mulhall, Wright, and others seem to believe that indigestion plays an important rôle; Glasgow, influenza; and Colins and Wright state that some general disturbance makes the patient susceptible to the development of the leptothrix or furnishes the proper nutrient material for the fungi present. It is impossible to state how far local morbid changes in the tonsil influence the production and course of the disease. A. Brown Kelly states: "In all the cases of 'pharyngomycosis' that have come under my notice chronic lacunar tonsillitis has also been present." Kraus and Garel believe that certain changes must take place in the mucosa before the development of the mycosis, this modification being brought about by some irritation, probably a catarrh.

The symptom which usually calls the patient's attention to the disease is the sensation of scratching, pricking, or stiffness about the region of the fauces. Some refer to more or less difficulty in deglutition. When the growths are prominent and come in contact with neighboring parts they may cause the sensation as though a foreign body were present. There may be, through the irritation of growths, more or less hawking and cough excited. Vocal fatigue is frequently mentioned. In one case under my observation, where the growths were situated at the base of the tongue, and so unusually prominent as to impinge upon the epiglottis, the scratching of that body caused its mucous membrane to be so inflamed as to give rise to exquisite pain in deglutition. Usually the condition is observed by the patient or his friends in the personal examination of the throat. When so seen it often excites considerable apprehension for fear that the lesion is diphtheria. On some individuals the discovery of the tufts makes no mental impression; others suffer great mental perturbation. There is no febrile reaction or disturbance of the general system.

An interesting feature of the disease is its tendency to undergo

spontaneous resolution, which occurs at a varying period from a few months to several years.

In considering the pathology of this interesting condition, and indirectly its etiology, it will be observed that from the earliest period of its known existence it has been supposed to be due to the presence of a parasite—varying types of the leptothrix buccalis. The early investigators seemed to be impressed solely with the finding of the parasite in the scrapings or the teased excrescences, not extending their investigations beyond this point. Efforts have even been made to produce inoculation, but without result (Heryng). A. Brown Kelly attempted to transplant the disease by direct inoculation of the crypts of his own tonsils, but without success. Decker and Seifert have claimed to produce the disease by the transplantation of the excresences. Heryng seems to have been the first who carried his investigation below the surface. He made sections of removed tissue and studied them. In this line of work he was followed by Colins and Garel. These investigators marked the transition period in the study of pharyngomycosis. Previous observers, satisfying themselves with the finding of an organism, proclaimed the disease without investigating the character of the surface exudation or the underlying tissues upon which it is implanted. Siebenmann, in his able exposition of the subject, carried us still further along this line of investigation. He made sections of removed quills, and also of tonsils with quills *in situ*. His examination showed the mass to be made up of a central narrow lumen containing bacteria, detritus, and mucous, surrounded by an epithelial wall, composed partially of layers of hardened, unnucleated epithelial cells and partially of a homogeneous, horny substance. On the outer surface of the quills which projected from the crypts were shown bundles of leptothrix. In the neighborhood there was absent every evidence of inflammation, such as hypertrophy of the connective tissue and small round-cell infiltration. In summing up his investigation he states as the result thereof that the process is an unusually intense cornification of the lacunar epithelium, which terminates in quill formation. He also states that keratosis of the tonsillar crypts in a mild form is not an unusual, but rather a common condition. He claims that the presence of the leptothrix is rather an incidental one, and bears no relation as a causative factor, as it is present in every mouth, and is usually deposited where the epithelial cells are the thickest. On account of the discovery of subepithelial buds, the absolute demonstration of the epithelial formation of the quills, showing only the manifestation of the spores on the outer surface, Siebenmann considers his case clearly demonstrated, and he desires that the name of the condition be changed to that of hyperkeratosis lacunaris.

Kelly in his paper, which was offered to adduce further proof of Siebenmann's contention, states that the disease known as mycosis leptothricia is, in reality, a keratosis; that the condition is more extensive than Siebenmann described; and offers the more adequate term to describe the condition—keratosis pharyngea. This paper by Kelly is a most able exposition of the subject, and well repays one for its perusal.

Among other things he states: "If one of the tonsillar or lingual excrescences be removed, when examined the surface is found to be soft, while the central part is tough and firm. Microscopically the soft substance is seen to be made of granular material, scattered through which are numerous long rods. The former are various micro-organisms commonly present in the mouth; the latter are leptothrix filaments." Later on he states: "While leptothrix filaments were abundantly present in the specimens obtained from the tonsils and tongue, and less so in those from the walls of the pharynx, they were never found in the excrescences taken from the nasopharynx." He also states that the excrescences examined showed that the disease in the nasopharynx and the oropharynx was identical.

"The excrescences in the nasopharynx presented a similar character to those situated elsewhere as regards appearance, firm adherence, tough consistency, and tendency to recur. Their structure was also essentially identical, namely, cornified epithelial cells, although the character of the cells differed in the two regions."

In summarizing he says: "First, nearly all the excrescences from the tonsil and tongue contain numerous leptothrix; second, the majority of the excrescences from the lateral wall of the pharynx contain no leptothrix; third, no leptothrix was found in any of the excrescences obtained from the nasopharynx; fourth, the abundance of the leptothrix in the excrescences varies considerably in different cases; fifth, when leptothrix filaments were present the first two varieties were usually found."

It seems hardly possible to think that a condition could exist in the nasopharynx and the lateral wall of the pharynx identical in the pathohistological changes to the disease which is also occurring in the tonsil and at the base of the tongue; and yet in one situation always showing the provocative, and in the other never showing this agent. I am more inclined to believe, with Siebenmann, Kelly, Chiari, and Kyle, that in the majority of cases of the occurrence the condition which we have above described—anywhere in Waldeyer's "chain of lymphatic glands"—is not due to the activity of the leptothrix, and that the leptothrix when present is simply an accidental deposit. Siebenmann has stated in his article, upon what authority I have no knowledge, that the leptothrix deposit is most pronounced where the

epithelial cells are more abundant. As I say, the above fact, which was brought out so strongly by Kelly and corroborated by all the other workers along this line, is, I think, the strongest point, independent of the histological change, that the condition is probably not due to the presence of the leptothrix. Another fact in favor of the condition not being dependent upon the presence of the leptothrix, and that it is a true keratosis, is the apparent subepithelial origin of the keratoid masses. Thus Siebenmann describes the subepithelial buds which are observed beneath the basement membrane, which, no doubt, by their growth push out toward the surface and develop the tufts. Such a condition has also been depicted by A. Brown Kelly, and he shows it in his article in an illustration. In this case there is a large empty cavity situated in the submucous tissue. The cavity is lined with epithelial cells, which apparently have no connection with the surface epithelia. At one extremity it shows cornified epithelial cells, and at the other extremity are congregated a number of round cells. Surrounding the cavity, and separating it from the epithelial layer, also, is an infiltration of small cells. An exactly similar condition has been observed in several of our specimens. In this the cornified epithelium is more marked than in the case represented by Kelly.

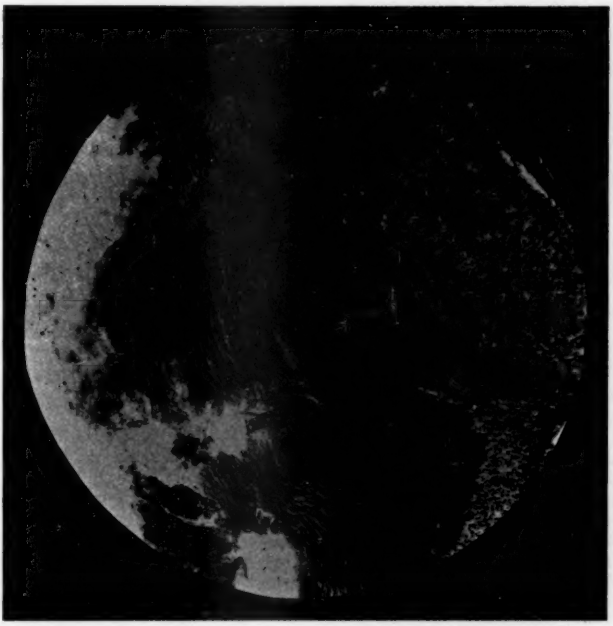
Kyle has also adduced facts to prove that the condition is a subepithelial one in that he has demonstrated that a peculiar fibrous band, extending from the subepithelial structures, penetrates and obliterates the basement membrane and extends out over the epithelial surface. This fibrous exudation, which forms on the surface, maintains its connection with the subepithelial structures, from which it obtains its nutritive supply.

Kyle states: "From the slides presented it looks as though whatever the pathological changes may be that they do begin from below and extend upward. The keratosis of the epithelial structures, whether it be due to some bacterial irritation as the causal factor, or whether it be associated with some epithelial change, at least is dependent upon the subepithelial structure, and the degenerative process, which takes place, as shown in the section, directly beneath the thickened areas on the epithelial surface, seems to affect these nodules, which, I think, furnish fairly reasonable ground for the deduction that the epithelial alteration is dependent upon the subepithelial change."

The description given by Heryng, Siebenmann, Kyle, Kelly, Tuttle, and Friedland, of certain histological changes in the epithelial structures, and confirmed by some desultory work on my part, seems to prove that there is a keratosis of the faucial and pharyngeal mucous membrane in the condition which is commonly known as pharyngomycosis.

It is also probable that the manifest changes begin in the subepithe-

lial structures. There seems to be no doubt that the change is identical whether appearing in the nasopharynx, pharynx, or faucial region. It is also apparent that the leptothrix is not a constant factor—*i. e.*, is most frequently found on tufts in the fauces, rarer on tufts from the pharynx, and never present on tufts taken from the nasopharynx. It is quite probable that the leptothrix is an accidental deposit, and has no causative relation to the structural changes. There seems to be no doubt that there is a condition in the pharynx, occurring in the very young and aged, attended with the presence of the leptothrix—a true mycosis; there is also no doubt that there is a condition occurring in



middle life which is not dependent upon the presence of the leptothrix —a true keratosis.

All the study I have made seems to correspond very closely with the reported work of the authorities quoted on keratosis. These facts so far adduced, while they clarify the atmosphere somewhat as to the condition of keratosis, have not been of much material aid as to the etiology of this condition. As it was apparent that the only way that satisfactory work could be accomplished along the line of a scientific study of the etiology and pathology of this disease was through the conjoint work of a clinician and pathologist, I have called

to my assistance, to do the most important part of the work, Dr. James Carroll. It would be impossible for me to offer any results of our work, so far made, without doing violence to their future value; therefore I am not able to go to any extent whatever as to our present findings. I add, as a present addition to this subject, a most excellent photomicrograph of one of our sections, which on study shows, without doubt, that however the change is brought about, the resulting pathological lesion is a keratosis.

These sections are all alike, except that some show the changes a little more perfectly than the others. This being one of the clearest specimens, I send it as an accompaniment to my paper.

On the surface of the mucosa will be seen the frequent piling up of the stratified epithelial cells, which evidently made up the tuft, which was broken at the apex by the pressure of the knife. Just below the stratified epithelial layer will be seen the thickened normal epithelial layer, and beneath that the tonsillar structure.

The photomicrograph demonstrates in a most perfect manner the actual keratoid changes which have taken place.

A PRELIMINARY STUDY OF THE OCULAR CHANGES PRODUCED BY THE INJECTION OF PURE CULTURES OF THE BACILLUS TYPHOSUS INTO THE VITREOUS CHAMBERS OF RABBITS AND GUINEA-PIGS.[1]

By Charles A. Oliver, A.M., M.D.,
of Philadelphia.

The results herein noted constitute but a portion of those that have been obtained by the writer during a series of experiments which have

[1] Read at the meeting of the American Ophthalmological Society, July, 1902.

Experimental work upon injections of chloride of sodium into the anterior chamber and into Tenon's space is now being tried in order to study the histological findings of any abortive effects that they may have upon the minor forms of bacteria invasion and inflammatory reaction.

General studies, both clinical and histological, to show the effects of vitreal colonization cultures upon other animals of similar kind and equal bulk are being prepared.

A series of experiments in an endeavor to show the routes of interocular lymph circulation are being made in a number of novel but strictly scientific ways. As early as is compatible for certainty of results the findings will be reported.

Culture studies from the mesenteric glands, the spleen, the liver, the bile, the bone marrow, and particularly the lymph channels of the cerebro-spinal system and its peripheral sense organs, will be made upon the visual structures.

Attempts at vitreous inoculation will be made upon animals which have been immunized as fully as possible in order to study the earliest and most minute evidences of local effects and thus to compare mere aseptic traumatic leucocytoses with pyogenic infections.

Instillations and injections of weak solutions of definite strengths of formalin, which drug is said to be a most excellent agent for killing the bacilli without disturbing the diagnostic qualities or the agglutinating signs, will be made upon induced mild cases of typhoid fever in the rabbit to determine whether the drug can be made of therapeutic value.

continued through a period of nearly three years' time.[1] In order to render the reading of the paper brief, logical, and intelligible, many details that are of value not only to the ophthalmologist, but also to the physiologist, the neurologist, and the general practitioner, have been omitted from the text of the report and relegated to foot-notes.

The type[2] of the bacillus employed was proved by the non-coagulation of milk with the ordinary tests; the inability to give rise to sugar fermentation with lactose agar; the absence of indol with and without the use of nitrites; and the production of alkaline reaction, or at least minimal degree of acidity, when associated with litmus milk before the micro-organism was used for injection purposes. To be doubly certain, the reactions to the blood serum of an immune animal and the agglutination tests were obtained.[3]

Pure cultures of the bacillus were injected aseptically into the upper outer anterior portion of the vitreous chamber of the animals, through a puncture made in the scleral coat, back of the ciliary region, mid-way between the insertions of the external and the superior rectus muscles.

The germ was inserted directly into the eyeball—ectogenously, as it were—a true primary bacillar infection, without any intermediate steps. The micro-organism was placed in a lymph organ which is in direct, close, and independent communication with the intracranial fluids.

The clinical expressions were rapid in their appearance. As a part of the general symptoms there were varying degrees of hyperpyrexia, lasting twelve to sixteen days. The animals soon refused food and lost weight, although carefully cared for. A number of them, particularly the rabbits, developed the characteristic signs of a true myelitis: some succumbed to toxin asthenia.

Locally, the iris became involved in from twenty to forty hours' time.

[1] Some of the primary work in these researches was done in the Pathological Laboratory of the Philadelphia Hospital, some in the Pathological Laboratories of the Department of Medicine of the University of Pennsylvania, and some at Wills Hospital. Many of the later experiments were performed in the private laboratory of the writer and at the home of one of his former assistants and friends, Dr. Van Schoick, of Hightstown, N. J.

In all, fifty-four healthy animals were studied; some twenty privately, twenty-four at the University of Pennsylvania, and the remaining number at the Philadelphia Hospital: of these, forty-six were rabbits.

The writer is under obligation to Dr. Simon Flexner, Napoleon B. Boston, Richard M. Pearce, and William F. Hendrickson for many suggestions throughout the studies. To Dr. I. L. Van Schoick and Clarence Van Epps he is grateful for assistance during the experiments. He is indebted to Dr. John T. Krall for most conscientious research work. He also desires to express his gratitude to Miss Mary C. Koonce, Miss Paula B. Himmelsbach, and Miss E. C. Potter for the execution of the many water-color sketches that have been rendered necessary in the proper pursuance of the work.

[2] For all of the primary experiments the human bacillus carefully obtained in pure cultures, and in some instances grown through several generations and proven to be still virile and able to reproduce the general disease, was used; rabbit cultures were employed in some of the later experiments.

[3] The cultures of these injection materials were kept *pari passu* with the series made from the intra-ocular fluids that had been aspirated at varying periods of time.

The primary manifestations consisted in a thickening of the stroma, the appearance of numerous radially arranged vessels, and the development of a number of clump-like hemorrhages at the major and minor circles. Scattered throughout the posterior chamber, and in the pupillary area, free erythrocytes mingled with fibrin and polymorphonuclear leucocytes could be seen. The retinal pigment layer of the iris was but little disturbed. The bloodvessels of the chorioid evidenced considerable injection, and in some situations the tissues of the membrane were œdematous. At this period a few deeply seated chorioidal and probably retinal hemorrhages, with fibrillary bands and dust-like opacities in the vitreous humor could be recognized.[1] The cornea was infiltrated in its deeper layers, and new blood channels sprang from the limbal series, penetrating the membrane in all manner of fantastic ways, but more often ranging in straight radial lines. In this stage, Descemet's membrane was found to be intact.

In a more pronounced stage, or as a separate condition, the conjunctival membrane and the subconjunctival tissues, especially around the corneoscleral junction, became œdematous and swollen, until in many instances the cornea was set in a deep and sharply circumscribed pit. The palpebral conjunctiva was but slightly affected, and the eyelids apparently did not participate actively in the process. The tissues around the point of inoculation were never more involved than were the other areas of inflammatory reaction. In many instances the vitreous chamber was in great part occupied by broad, yellowish masses, which reached almost as far forward as the posterior capsule of the lens. A number of these cases showed a beginning increase in intraocular tension. Early in this stage the retina evidenced such extensive infiltration with leucocytes of polymorphonuclear type, that all appearance of retinal structures often was obliterated. Considerable extravasation of red blood cells into the tissues could be determined in some situations.[2] There were many accumulations of inflammatory exudate, serum, leucocytes, and erythrocytes.

Grosser forms exhibited an increase of all of the previous conditions, with a number of superadded signs of coarse, degenerative type. Portions of the corneal epithelium were denuded, the underlying lamellæ exhibiting minute areas of necrosis. The iris showed numerous thickenings, discolorations, and, rather infrequently, a few fine plastic lesions. The lens[3] and the capsules were opaque and tumescent in places. The

[1] No qualitative blood studies have been established as yet.

[2] In some places the amount of exudate of serum and corpuscular elements was so marked that the retina was found to be separated from the chorioid, giving an appearance resembling ordinary blisters.

[3] The crystalline lenses have been set aside for special study, though the presence of the bacillus in these structures has been proved by pure growths obtained in culture colonization.

external structures were much swollen and catarrhal. There was a true lessening of intra-ocular tension.

The last stages exhibited numerous atrophic signs. In many of the first cases studied, the eyeball had shrunk into a small, irregular, and hardened stump, fixed in a mass of coarse, fibrinous tissue. Over this crossed the remnants of a cicatrized and band-like conjunctiva, dragging the thinned and irregularly shaped lids against itself.

At varying periods during the many stages of these reactions, minute quantities of the infected vitreous humor were carefully aspirated and placed in various culture media. Most of these withdrawals were made through the corresponding inner sides of the anterior segments of the eyeballs.[1]

Cover-slip preparations of the withdrawn vitreous fluids showed motile typhoid bacilli, with peritrichially arranged flagella, these bacteria exhibiting their peculiar properties of not being able to retain aniline dyes when treated by the Gram or Weigert methods.[2]

In many, if not in all of the cases, the infected portions of the withdrawn vitreous humor were found to be translucent where filled with bacilli. Nearly all of the specimens of removed aqueous humor were more or less albuminous in character.

After preparation of the tissues in different ways several hundred sections showing the combined effects of the germ and the traumatism upon all of the ocular tissues were obtained. These specimens were studied in every detail.[3] The main characteristics were as follows: In sections of the early stage, portions of the ciliary bodies and adjacent uveal structures—probably the glandular tissues—were swollen, and in some instances were found to contain aggregations of typhoid bacilli. Penetrating and surrounding these tumescent parts were numerous dilated capillaries and newly formed bloodvessels, from which the typhoid bacillus could be isolated in a number of instances. In direct connection with the lymph organs there were numbers of large, free masses of the bacilli. Further back, the superficial layers of the retina were found to be richly infiltrated with polymorphonuclear cells and leucocytes. As early as the fourth day free hemorrhages were found irregularly distributed throughout the fibre layer and deeper

[1] The rule that was made was that, although different amounts of the material were injected, yet the most minute quantity possible was withdrawn.

[2] Attempts for agglutination processes within the ocular bulb (which is particularly rich in lymph glands), showing the effects of development, growth, and colonization modifications upon the already inflamed contiguous structures will be tried, not for diagnostic purposes, but for actual therapeutic gain. For this purpose variable strengths of dilute serum will be employed. Widal's reaction studies will be applied to this particular phase of the work.

[3] These studies have nothing whatever to do with the many post-febrile conditions which are so constantly quoted as being associated with and following typhoid fever, and which at best are merely concomitants and sequelæ of any form of continued hyperpyrexia. Such conditions cannot be considered as pathognomonic of the disease.

portions of the retina, particularly in the circummacular regions, just below the outer extension of the normally retained nerve sheaths of the animal.[1] Rather deeply placed and more forwardly situated hemorrhagic extravasations from the two inner vascular layers of the chorioid were found in two or three of the cases.

There were not any coarse indications of pyogenic infection in this grade of sections.

In the grosser stages, many of the sections showed an acute endarteritis in association with the bacilli.[2] Some of the specimens exhibited changes that indicated toxin action; others[3] evidenced signs of well-marked secondary infection. In the majority of the non-lethal cases sanguineous extravasations with some erythrocytic aggregations and leucocytic masses were seen. At times, hyperplasia and even degenerative changes in the adjacent tissues were manifest. In some of the cases, both arteritis and periarteritis and phlebitis and periphlebitis could be seen near the larger lymph cavities and main lymph channels.

In the coarser groupings, there were all the marks of erosion of the walls of the larger vessels, with gross signs of pyogenic invasion throughout the now greatly disorganized tissues. In the equatorial sections especially, secondary phlebitis with streptococcal and staphylococcal invasion of the clots and venous coats—true sepsis—could be determined. Many thrombi composed of fibrin-laden leucocytes, situated mostly in the lymphatic channels and main venous stems, could be seen, the containing walls in places being excessively attenuated. In the more marked cases there were localized abscesses. Pyogenic micro-organisms were obtainable in excessive amounts in nearly all of the ocular tissues.

The last stages showed all manner of connective-tissue growth. Well-pronounced foci of cell death—leucocytic in part—surrounded areas of necrotic tissue, which at times were almost indeterminable. The bacillus typhosus was now most difficult to find, only an occasional stray one being seen.[4]

[1] Rabbits.

[2] This finding substantiates Keen's belief in microbic invasion as the cause of retinal hemorrhage.

[3] Not many signs in this stage of the condition.

[4] True optic neuritis was often present in cases in which the eyeball was destroyed, but in most instances it was of pronounced type, and it never involved the fellow organ. Several times a very low grade of the condition, as secondary to uveitis, was seen ophthalmoscopically. In this connection it must be remembered that the primary invasion of the germ was through the eye.

The presence of the germ in the meninges and the linings of the lymph channels of the brain was more than once noted during the cursory examinations vouchsafed these structures by the writer.

In the vast majority of cases, oculomotor changes in typhoid fever are dependent upon intracranial disturbance, but it is conceivable, nay, probable, that a true peripheral neuritis from the actual presence of the bacillus typhosus and its frequent associates, particularly in the vascular and lymph channels of the muscular and other tissues of the orbit, can give rise to

Bacteriological examination of the inflamed conjunctivæ showed true secondary infection; pneumococci, staphylococci, and streptococci being present in the tissues, fluids, and secretions. Orbital involvement was not infrequent.

In one of the cases which had progressed from a slow form of suppurative panophthalmitis to a phthisical globe, the bacillus typhosus was found nested in the extra-ocular orbital contents in several situations, substantiating Swanzy's belief concerning the same and proving Panas' findings.[1]

In a word, every portion of the organ is affected.[2] The ocular expressions of the presence of the germ are protean and panophthalmic; the low-grade uveites, keratites, and retinites being principally primary, and the ophthalmites, gross conjunctivites, and orbital cellulites mainly secondary.[3]

REMARKS. Presupposing that the tissues or "soils," as they are called, were as near alike as possible, the symptoms varied with the dosage.[4] The majority of the eyes perished with the amounts of injections at first used. Later, with the employment of lesser amounts and the same technique, most of the eyeballs, though ofttimes functionless, were saved. In a few, the symptoms subsided early, and the eyes were able to functionate.[5]

localized peripheral palsies and trophic changes. Of course, true extension of pyogenic inflammation along the nerve, vessel, and lymph channel tracts may take place from contiguous areas of primary bacillar inflammation, and as a result no bacilli be found in the extra-ocular structures.

[1] Since the time that the main experiments were made several cases studied by the writer showed that the other eye could be made to participate in the characteristic manner of typhoid inflammation by an injection of a slight amount of streptococcal matter into it, true typhoid germ colonization areas being found in the interior of the organ, thus proving in a measure the earlier finding, that a few stray bacilli from endogenous infection may produce fine retinal and chorioidal hemorrhages in the constitutionally affected organ.

[2] Traumatic infection during the experimental procedures, in the minor cases at least, can be set aside to some extent by the presence of the germinating bacillar colonies in the vitreous humor, the absence of pyogenic germs, and the distinct localization of the leucocytoses around the typhoid organism aggregations.

[3] In these two varieties there is merely an induced ocular type of the general disease. The fever may be induced by the primary entrance of the bacillus typhosus into the structure of the eyeball, not only giving rise to local effects, but also to general disturbances. This is particularly true in cases in which there is an already existent streptococcal invasion of the ocular bulb or surrounding lymph channels. It will thus be seen that it is possible to have a localized typhoid bacillus disease of the eye without general involvement. Introduced directly into an eyeball, either accidentally or intentionally, the micro-organism may germinate locally only and excite leucocytosis and bactericidal action of the serum and the blood to a sufficient degree to produce a primary infectious condition before being destroyed or rendered innocuous. Particularly is this so in cases in which lymph and consanguineous circulations are impeded, as, for example, in glycosuria and glaucoma.

[4] The bacillus typhosus belongs to what is known as the facultative anaërobic type—that is, it is a form of life which, while growing the best with a plentiful supply of oxygen, is able to exist with but a very small amount and even none at all.

[5] The well-known fact that typhoid fever bacilli can be carried within the human body for many years makes it entirely within the province of certainty that the germs may remain dormant, or even isolatedly colonizing very slowly and indefinitely in successive generations,

Experimentation showed that the bulk of the early intra-ocular conditions arose from the processes set into action by the actual presence of the typhoid bacilli themselves, and that they were not dependent upon a minor aseptic traumatism.[1] Vessel-wall erosion with hemorrhagic extravasation, lymph-gland infiltration with lymph- and blood-stream blockage, and increased leucocytosis with an abundance of the germ element were soon followed by the formation of bacillar colonization areas, giving rise to a punctate haze, with fibrillar opacities in the vitreous humor,[2] succeeded in turn by inflammation of the bacilli-laden coats of the ocular vessels. Thrombi appeared and leucocytosis became profound.[3]

The second stage—one of localized septicæmia in which suppurative processes, not only from the typhoid germs themselves, but also most probably from ectogenous inoculation through ruptured channels, ensued—pyogenic micro-organisms became prevalent and most virulent. At this period the bacillus typhosus began to disappear.

Later, the tissues degenerated; perforation through the ocular coverings, both from within and without, took place; the eyeball atrophied, and cicatrization bands of connective tissue, tying the organ into a motionless nodule, formed.[4]

Should the ocular conditions be less pronounced, and the lymph channels to the brain remain pervious and active, intracranial and spinal infections from the passage of the germ and its associates will early ensue, giving rise to all manner of coarse clinical signs of central disease.[5]

The minor degrees of endogenous type—in which there are slight and at times undisturbing and unsuspected retinal and uveal symptoms, as so frequently seen in the primary intestinal forms of the disease—are interesting, and prove what has been claimed ophthalmoscopically by a few competent clinicians.[6]

within the eyeball for long periods of time. In such situations they may remain harmless until discharged into seral circulation by some traumatism or secondary degeneration of the surrounding tissue. For aught the writer knows the bacillus may yet be present (seven months at present writing) in the shrunken eyeballs of two rabbits which are being kept alive for other purposes.

[1] Coarse pathological examination cannot explain the etiology of the condition. Careful histological and bacteriological research, as in these studies, must always be instituted. The best results are obtained in cases in which there has been but a moderate degree of reaction

[2] Both Bull and Hansell describe this condition clinically.

[3] About this time general leucocytosis is most marked.

[4] In cases in which the animal had recovered from the gross local and general clinical signs of the primary vitreous infection, the second eye, when experimented upon, did not behave so badly as its fellow, this probably being due to the presence of germicidal serum in the vascular channels, or possibly even in the serum of the tissues of the animal.

[5] This may not be an infrequent cause for lethal result. The effects of the bacillus upon the intracranial prolongations of the visual apparatus will be considered in another communication. Nissl's method will be employed in a part of this work.

[6] It is possible that some of the cases of suppurative ophthalmitis occurring during attacks of typhoid fever, or even when individuals are exposed to infection from others, have arisen

The external ocular signs, which have been not infrequently described as associated with the general disease, can all be placed under the same categories of cause and effect, and are mere expressions of the main conditions.

The position in regard to the pathology that may be taken is that when the bacilli-laden serum gets into the interior of the eyeball, agglutinative processes followed by bacteriolytic changes which remove the bacilli take place. This destruction frees the toxins, which are either carried away or neutralized by the antitoxins. During these changes the invaded structures of the eyeball lose a few or many of their component parts, with the final result of either a useful organ, a functionless one, or a mere mass of degenerate tissue.[1]

PERFORATED GASTRIC ULCER; PERITONITIS; DEATH; DIAGNOSIS AT AUTOPSY.

By Astley Paston Cooper Ashhurst, M.D.,
Resident Physician at the Episcopal Hospital.

For permission to report the following case I am indebted to my chief, Dr. D. J. Milton Miller, in whose service at the Episcopal Hospital it occurred:

Kate J., single, white, aged fifty-seven years, occupation governess and companion, applied on January 29, 1902, for admission to the Episcopal Hospital, complaining of general malaise and a cold on the chest. She had been much interested in the work of the hospital about

from the actual entrance of the bacterium into the eyeball itself through a break in the ocular tissue—a true ectogenous infection. It is probable, as hinted in another place in this communication, that the auto-infectious cases suffer the less—that is, if the general condition is relatively good.

[1] It is highly probable that the soluble toxins of the streptococcus diminish the protective leucocytosis of the organ. If not early destroyed by the bactericidal power of the serum and blood, they will permit a rapid growth with increased virulence of the typhoid germs, producing not only suppurative death of the organ, but also pronounced involvement of the cerebro-spinal cavities. Fortunately, in most cases of general typhoid invasion the streptococcal elements, unless locally introduced, are so frequent in the ocular bulbs that gross localized affections of the eyeball from the actual offensive presence of the typhoid germ are seldom seen.

It is probable that most of the reported instances of destructive eye changes in cases of typhoid fever have had previous or coetaneous breakages of the ocular walls, with the entrance of streptococcal material, the toxins of which have aided the bacilli to act much more decidedly, and thus give rise to expressions which could be recognized by coarse clinical study; conditions which perhaps have been simply superadded to existing signs of the disease, such as retinal and uveal hemorrhages.

In the intestinal type of the disease the micro-organism probably germinates in the lymphatic glands and then enters the lymph and blood circulation. In these researches the serum is thrown directly into one of the nearest, one of the most direct, and one of the largest lymph streams passing into those within the intracranial structures; thus probably giving rise to a more rapid and a more pronounced symptomatology of the nervous system than could be found in any other variety of ectogenous infection.

twenty-five years ago, and it was owing chiefly to her antecedents, and not because she seemed particularly ill, that she was admitted to the medical wards under the diagnosis of chronic gastritis and debility. She particularly requested that she should not be required to go to bed, as she did not feel sick enough for such confinement, but merely wished warm housing and good food.

Family History. Mother died of cancer of the uterus at fifty-six years of age; stepfather (with whom she had always lived) of "slow consumption," at about fifty years of age; one sister at the age of about forty years, of carcinomatosis; and another sister, at nineteen years, of consumption. Two brothers and two sisters are living and well.

Previous History. As a child she had measles and whooping-cough. Never had diphtheria, scarlet fever, pneumonia, typhoid fever, tonsillitis, or rheumatism, and was always considered the healthiest member of the family.

Present Illness. Patient felt perfectly well until Sunday, January 5, 1902, on which date she says she "gorged herself with roast duck." She felt, however, no immediate inconvenience; did not vomit, and had no particular gastric distress; but from that time gradually lost her appetite, and became unusually constipated, so that her bowels were not properly opened for a week. She then took some citrate of magnesia, and for several days had three or four quite normal movements daily. For the last few days the patient says she has had her bowels opened five or six times daily, the consistency of the fecal evacuations being normal. She complains now of flatus and of abdominal cramps; feels chilly; coughs occasionally, and is rather hoarse.

Physical examination shows a thin, slightly jaundiced woman, well past middle age, with dry, fissured tongue, covered with flakes of mucus. The throat is full of mucus; there are no patches; the tonsils are not enlarged. The chest is spare. There are no areas of dulness in the lungs, but expiration is slightly prolonged posteriorly. The heart is negative. The abdomen is held very tense, is tympanitic, slightly distended, and is tender in the hypogastrium. The spleen and liver are not palpable.

The urine was of specific gravity 1015, and was acid. There was a fair reaction for albumin; none for sugar. A few broad hyaline casts were present. Her temperature was 98.8° F.; pulse about 65; respirations, 28.

In making my rounds the next morning I found the patient upon her hands and knees in the bed; she complained of no pain, but said the wind in her stomach made it impossible for her to breathe comfortably while lying on her back. Her bowels had been partially checked by full doses of bismuth subnitrate. When I returned to her, after going through the other medical wards, she was able to lie down quite comfortably. There was no change in her condition to be detected, but she did not feel disposed to be out of bed. During the afternoon she rested comfortably and slept at times. In the evening she complained of cold feet, and was given hot-water bags. Her temperature was 98.5° F., her pulse was 60, and her respirations 30 per minute. The pulse in her left radial, which I had not noticed before, was very feeble, due, perhaps, to her position in bed, but that in the right was normal. She lay on her left side most of the time. I saw her again

when making my night rounds at a little before 1 A.M. on January 31. She complained then of having had some sharp pain in the stomach, but this was relieved by the next dose of bismuth. She said she had been sleeping and would soon be asleep again. Once after this the nurse took the patient some milk, but at her second subsequent visit found her apparently dead. When I reached her bed a few minutes after 3 A.M. she was lying on her left side as when I had last seen her; she had evidently been dead some time; her extremities were cold (although her body was still warm), and there was slight rigor mortis.

The autopsy was made about fifteen hours after death by Dr. W. E. Robertson, the pathologist of the hospital, who has kindly allowed me to abstract the following notes from his records:

The body is that of an emaciated woman; rigor mortis marked; subcutaneous fat and musculature much wasted.

Abdomen. Over two quarts of foul-smelling, greenish, purulent fluid in the peritoneal cavity; the small intestines are agglutinated by bands of lymph probably forty-eight hours old; the appendix is normal; there is no Meckel's diverticulum; the mesenteric glands are enlarged and hard. The stomach presents, high up in the lesser curvature, a perforated ulcer opening into a ruptured abscess cavity formed beneath the left lobe of the liver by adhesive inflammation; the lesser peritoneal cavity is full of this purulent fluid, and on the posterior surface of the stomach near the lesser curvature and close to the œsophagus there is a second perforated ulcer, separated by the lesser omentum from that first described; extending from these ulcers around the greater curvature of the stomach is a mass of cicatricial tissue dividing the stomach into two pouches, the pyloric being the larger. The liver is extremely pale, and in the right lobe there is a transverse constriction, forming one of the typical forms of corset liver; on section the liver is nutmeg in appearance. The kidneys are paler than usual, but normal in other respects.

Chest. The pleuræ present numerous bands of adhesions, well organized; the lungs show hypostatic congestion in the bases, and at the apex of the right lung is a healed tubercular area. The heart is normal.

The chief points of interest in any case of gastric ulcer, apart from therapeusis, are briefly—the possible causes, predisposing or exciting; the symptoms during life; the duration; the number, size, and site of the ulcers; the mode of death—by perforation or by hemorrhage; and if by perforation, whether previous adhesions had prevented immediate peritonitis.

Among predisposing causes, sex alone is typical in the present case—60 per cent. of all cases are said to occur in females.[1] The age is here distinctly atypical, although the ulcer may have first formed when the patient was young—gastric ulcers occur in women under forty years of age in over 77 per cent. of all cases,[2] the average age in one hundred and eighty-seven women thus affected having been twenty-seven and one-tenth years.[3] Occupation may be considered a predis-

posing cause, it being generally said that among women, domestic servants and dressmakers, and among men, cobblers and tailors, are most liable to the disease; yet, investigations upon this point have failed to confirm the accepted idea;[3] but the physical habits of a governess are sufficiently near to those of dressmakers to render the occupation in this case worth observation. Tuberculosis was formerly considered a predisposing cause, and this patient had healed tubercular lesions in her lung; but, on the other hand, it has been shown that the incidence of tuberculosis among cases of gastric ulcer is not greater than among the community at large.[4] Disturbances of the menstrual function may in this case be excluded, as she had long since passed the menopause.

Other causes to be considered are a hyperacidity of the gastric juice, or an alkalinity of the blood less than normal; the possibility of thrombosis or embolism of the gastric arteries, or of extravasation due to portal obstruction. In the present instance no observations on the blood or the gastric juice were made; but the great deformity of the liver suggests the possibility of interference with the gastric circulation, either directly by pressure,[5] or indirectly through the medium of the portal vein. Chambers[6] calls attention to "those habits of half-civilized life which they (women) persist in, such as wearing ill-fitting stays, with rigid beams in front, pressing upon the viscera; leaning forward to work immediately after food; swallowing their food half masticated," etc. But if mere portal obstruction were a cause, as suggested by Virchow[7] might be the case, cirrhosis of the liver would not be such a rare complication as it is.[8]

In the present case there were no symptoms known to have existed during life, except anorexia for a few weeks immediately preceding the fatal termination. This is by no means an unusual experience.[9] Cruikshank[10] narrates a case in which a young lady died after two or three days of illness, having previously been in perfect health. "I was called in," he says, "but she was dead before I got to the house. From her history I was at a loss to account for her death; but on opening the abdomen . . . I found the contents of the stomach in that cavity; they had produced peritoneal inflammation, and killed. On examining the stomach, I found a hole in it large enough to admit the end of my finger. This hole had been formed by . . . ulceration; its edges had adhered by inflammation to the under surface of the small lobe of the liver . . . If no violent vomiting had taken place and torn this adhesion at this particular time, she might have lived for years, notwithstanding the ulcer."

The duration of this ulcer, from the partial cicatrization, with the thickening and induration, and the hour-glass contraction of the stomach, must have been for many years, but the history of the patient

throws no light on the subject. It is said by some authors that perforation is less usual in ulcers of long standing than in those of recent formation, inasmuch as the inflammatory reaction thickens the base as well as the walls of the ulcer,[17] and Welch speaks of the "acute perforating ulcers" as of a distinct variety.

TABLE I.—SHOWING SITE OF GASTRIC ULCER IN GENERAL.

Author.	Anterior wall.	Lesser curvature.	Posterior wall.	Pylorus	Fundus	Cardia	Anterior posterior walls.	Greater curvature.	Total.
Brinton[7]	10	56	86	32	0	4	13	5	206
Welch[1]	69	288	235	95	29	50	0	27	793
Per cent.	8	34.4	32.1	12.7	2.9	5.4	1.3	3.2	99/100

TABLE II.—SHOWING SITE OF PERFORATED GASTRIC ULCERS.

Author.	Anterior wall.	Lesser curvature.	Posterior wall.	Pylorus	Fundus	Cardia	Anterior posterior walls.	Greater curvature.	Total.
Bidwell[19]	36	2	8	0	0	0	1	0	47
Comte[19]	28	4	8	3	0	0	0	0	43
Per cent.	71.11	6.67	17.78	3.33	0	0	1.11	0	90/100

The number of ulcers is usually single, Brinton reporting multiple ulcers in 21 per cent. of a total of 536 cases;[18] and while the size is generally that of a pea or a dime, some very large ulcers have been recorded; that in this patient seems to have completely encircled the stomach, except beneath the lesser omentum, on each side of which a perforation occurred. Multiple perforations appear to be distinctly rare, probably because the patient either dies from the first, or has other threatening perforations invaginated at the operation undertaken for the repair of the first to perforate. In a case recently reported by Mayo Robson,[11] two perforations were found, that for which the operation was performed being found beneath adhesions on the anterior surface of the pylorus, while the second, discovered by accident, as it were, through the incision into the pylorus, was on its posterior wall, and had perforated into the pancreas. In regard to the site of the ulcer, various statistics have been published; but it is not always stated clearly whether the figures refer to all ulcers, or only to ulcers which have perforated, and even in regard to the last-mentioned class observations are not in accord—thus Welch quotes Brinton as stating that of 100 ulcers on the anterior wall of the stomach 85 will perforate; but, says Welch,[1]

on account of the infrequency of ulcers on the anterior wall, perforation actually occurs oftener in other situations, particularly in the lesser curvature and near the pylorus; yet it may be seen in the accompanying tables that, although ulcers most frequently are found on or near the lesser curvature, nevertheless, perforations are most frequently found in the anterior wall.

Although the numbers in the second table are less than one-tenth of those involved in the first, yet the difference in the results is so great that the relation could scarcely be materially disturbed, even were the number of perforations recorded to equal that of the total number of ulcers observed. The second table should prove of special interest to the surgeon.

Osler[12] says that when situated in the lesser curvature, or, more correctly speaking, near the lesser curvature, since, as remarked by Rokitansky, an ulcer is rarely directly upon this portion of the stomach, but usually to one side; when in this situation, ulcers are usually nearer the pyloric end than close to the œsophagus, as in the case now reported. Perforation is stated to occur in from 3 per cent.[3] to 13 per cent.[14] of all cases—it is to be hoped that the more recent smaller percentage shows an advance in treatment; and adhesions occur in only about two-fifths of the perforations;[14] moreover, perforation is much more apt to occur in women than in men, and in three-fourths of the cases the woman is under thirty-five years of age, while in males this accident appears to be equally divided among all ages, though less frequent after fifty years.[7] In the present case, therefore, perforation, had an ulcer been known to exist, should not have been anticipated. Adhesions form to the liver only about one-third as often as they do to the pancreas,[4] even when situated near the lesser curvature.

The latency of all symptoms in the present case, even after fatal peritonitis had developed, is not the least remarkable feature. It seems probable that the ulcer on the posterior wall of the stomach perforated first, possibly after the patient's heavy meal on January 5th, that she carried the abscess thus formed in the lesser peritoneal sac (which Welch speaks of as a rare occurrence) without much disturbance until after her admission to the hospital, the general peritonitis only forming then upon the rupture of the abscess formed beneath the liver by the anterior perforation. Possibly she had developed by this time a tolerance for peritoneal inflammation, through slow absorption of the toxins.

There was recently in this hospital another fatal case of peritonitis, from appendicitis in a youth, the inflammation having lasted probably a week, though the history was somewhat obscure, in which, although there was movable dulness in the flanks, and although other physical signs of a diffuse suppurative peritonitis were obtained, yet the tem-

perature, which was 98° F. on admission, remained at that point for over ten hours, when it first began to rise, never exceeding, however, 99.5° F.; and the pulse, full and strong, ranging from 78 to 88 per minute. There was also a case of fracture of the base of the skull, admitted last spring, in which at the autopsy was found a rupture in the stomach, with diffuse peritonitis, yet, through the four days before death the pulse had been about 90, and the temperature never above 99.5° F. Of course, in this last case the concomitant injury to the brain may have affected both pulse and temperature, yet it seems undeniable that too much reliance should not be placed on these as an index in cases of possible peritonitis, especially by hospital residents, but that more pains should be taken to make an accurate physical examination and to acquire the *tactus eruditus*.

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MALARIA: A SUMMARY OF RECENT PROGRESS IN THE KNOWLEDGE OF ITS ETIOLOGY AND PROPHYLAXIS.

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THIS disease, from its far-reaching effects, the most important we meet in tropical practice, is not limited by any geographical boundaries, but appears in all or nearly all parts of the globe.

In the temperate and far northern countries it is usually mild in character, and by far the greatest number of these cases are those of benign quartan or tertian infection.

It is only in tropical or subtropical countries that we see the ravages of this disease in its malignant and pernicious forms.

It undermines the health of millions of native inhabitants, stands in the way of European or American colonization, invalids the greater majority of those on the sick list of our army and navy, and is responsible, either primarily or secondarily, for a larger death-rate than any known disease of these latitudes.

HISTORY. It has been known and described for several thousand years; 100 B. C., Varro, a Roman physician, stated that it was produced by inhaling or swallowing a small animal which grew in the marshes.

Since that time, and until very recently, it has been regarded as a place disease, of typical miasmatic origin.

The first stride toward our present knowledge of the disease was made in 1880, when Laveran discovered in the blood of malarious patients the plasmodium which bears his name; that this organism is the cause of malaria was quickly verified by careful experiments made all over the world.

Later, in 1885, Golgi described the life-cycle of the organism in man, and pointed out its relationship to the periodicity of the febrile attacks.

In the *Lancet*, November 13, 1897, MacCallum, of Baltimore, described the function of the flagellum (migrogamete).

In the following year, 1898, Major Ross, of the Indian Medical Service, a pupil of Manson, who, for several years past, had been at work upon the latter's theory of the rôle played by the mosquito in malaria, was able to announce the life-cycle of the parasite in a certain species of mosquito, the Anopheles claviger.

Since then the work of Celli and others in Italy has substantially emphasized the value of these investigations; it is now a certain and generally accepted fact, that malaria is produced by the bite of an infected mosquito of the genus Anopheles.

THE MALARIAL PARASITE. In zoölogy the plasmodium of Laveran is classed among the Protozoa, of the order of Sporozoa, and is closely allied to the suborder of Coccidia.

They consist of true cellular elements, protoplasm, nucleus, and nucleolus; they are possessed of amœboid movement, and multiply by sporulation.

They are true parasites, and live at the expense of the red corpuscles.

Their life-history is divided into two cycles: one in the blood of their human host, which is asexual, and the other in the body of the mosquito, which is sexual. Judging from clinical observations, it is possible that there is a third state of their existence, a latent state within the human organism. If not, how can we explain the malarial manifestations which occur in those who have suffered from the disease, but from whose blood the parasite has been absent for months?

Celli recognizes but three distinct species of the malarial organism, the benign quartan and tertian, and the malignant tertian, or Æstivo-autumnal, of the Italians; Manson, on the other hand, describes five, which he classifies as follows:

Benign	Quartan Tertian	do not form crescents.
Malignant	Quotidian—pigmented Quotidian—unpigmented Tertian	form crescents.

All these as a class have certain characteristics in common; beginning with the time they enter the red corpuscles and grow and live at the latter's expense.

At first the pigment is scattered through the protoplasm, the latter becomes agitated, the pigment arranges itself in the centre, the protoplasm arranges itself in stellate form about the centre, each filament containing a new nucleus, fission begins, the wall of the now destroyed red corpuscle is ruptured, sporulation is complete, the spores escape into the serum, and a new era commences.

Now and then you will see a large spherical parasite escape from a red corpuscle, some of which in a short time become violently agitated, finally throwing out flagellæ, others more granular in appearance remain spherical. The former are the microgametocytes, the flagellæ they throw out the microgametes, or spermoids; the latter are the macrogametes, or ovules, which later, in the stomach of the mosquito, become fecundated by the microgametes, or spermoids, thus continuing the life of the parasite in its extra-corporeal host.

Going into the specialization of the various forms of the parasite, we find that all of them observe this general procedure, differing only in detail.

Quoting Golgi, first taking the benign quartan, we find it to have the following characteristics.

1. It completes its asexual life-cycle in three days (seventy-two hours).

2. It invades nearly the whole red corpuscle, but does not enlarge or discolor it, even when it has almost entirely filled the red corpuscle.

3. The amœboid movement is rather sluggish; the form does not change much while under observation. The contours of the parasite are readily distinguished from the rest of the red corpuscle.

4. The pigment consists of coarse granules, having feeble movements.

5. Toward the end of apyrexia the pigment collects in the centre, and fission or formation of the amœbulæ begins. These are from six, twelve, to fourteen in number; frequently, when the pigment is in the centre, the amœbulæ are arranged around it in a daisy-like form.

The principal characteristics of the benign tertian are—

1. It completes its asexual life-cycle in two days (forty-eight hours).

2. It invades the whole of the red corpuscle, which becomes large and pale. Frequently it is rather difficult to differentiate the contour of the parasite from the edge of the red corpuscle which surrounds it, because of the extreme paleness of that cell. The loss of color of the red corpuscle takes place while the parasite is still small.

3. The amœboid movement is very active, the changes in form of the parasite are quite apparent, and, while watching it, pseudopodia can be seen to be rapidly protruded and retracted.

4. The pigment consists of fine granules, which move actively.

5. Toward the end of apyrexia, the pigment tends to collect in the centre, and multiplication begins.

The number of amœbulæ is usually greater than of the quartan, consisting of from twelve to twenty.

THE MALIGNANT PARASITE. These are very much smaller that the benign parasites, and for this reason, and to the fact that their pigment is much finer, they are much harder to distinguish.

At first they display very active amœboid movement, but quickly quiet down, and appear as minute bright rings, frequently several in number in the red corpuscles; later in the disease it may be a difficult matter to find even these in the blood from a pricked finger or ear, and even more difficult to find the parasite in its later stages of development; it being necessary to get aspirated blood from the spleen for diagnostic purposes.

We also find in the blood of patients suffering from maligant malaria, crenated, warped, dark-colored corpuscles known as the "brassy bodies;" these are produced by the rapidly necrotic action of the parasite upon the red cell.

The most characteristic feature is the presence of crescents, which are only produced by malarial parasites of malignant type, and are, therefore, absolutely diagnostic. They do not appear in the blood during the early days of the disease, but usually only after the lapse of a week or more. After all traces of fever and the small parasites have disappeared, these crescents persist in the blood, sometimes for two or three weeks, and are usually associated with cachexia.

Some of these crescents develop in the following manner: first the crescent becomes an ovoid, with the pigment scattered through the mass; this in turn becomes more or less rounded, or spherical, then the pigment forms a ring about the centre, then finally approaches the periphery, the whole parasite becomes violently agitated, throwing out flagellæ, which have a wave-like motion, many of which break away, and we have the microgamete, or spermoid.

Others simply advance as far as the rounded or spherical formation; these are the macrogametes, or ovules.

The parasite of malignant quotidian malaria is very small, and consists of two varieties, pigmented and unpigmented, and develop much in the usual way; they occupy when mature about one-third or one-fifth of the red corpuscles, and sporulate in twenty-four hours, giving rise to six or eight minute spores.

Those of malignant tertian resemble in many respects the parasite of benign tertian, although much smaller, occupying about one-half to two-thirds of the red corpuscle; at the end of two days (forty-eight hours) they sporulate, in number about eight to twelve. The distinguishing features of the malignant parasites are the formation of crescents, and the small size of the parasites.

Life-cycle in the Mosquito. In the stomach or middle intestine of the mosquito, at a temperature of 86° F., the microgametocyte will throw out the microgamete, or spermoid, within the first twelve hours; numbers of these wriggle toward one of the macrogametes, or ovules, which upon their approach becomes violently agitated; finally one of the spermoids effects a successful entrance, and fecundation is completed.

These fertilized bodies, known as zygotes, assume various shapes, usually that of an elongated ovoid; they now penetrate the epithelial cells of the middle intestine; this, as a rule, takes about forty hours.

By a process of direct division, multiplication of the species takes place, and the zygote becomes greatly enlarged, and projects into the general body cavity of the mosquito. When this process is completed, taking about seven or eight days, the sac ruptures, discharging into the general body cavity, a large number, about ten thousand fusiform bodies, known as sporozoites.

These, by means of the lacunar circulation, find their way to the salivary glands of the mosquito, where numbers of them collect, and are injected into the blood of man through the insect's proboscis. Here they at once enter the red corpuscles, and complete the life-cycle we have already described.

The Genus Anopheles. As this is the only mosquito capable, by its bite, of producing malaria in man, a description of this genus alone is necessary here.

There are four varieties that are able to do this, viz.: the Anopheles claviger, the Anopheles superpictus, the Anopheles pseudopictus, and the Anopheles bifurcatus; the first and last varieties are abundant in all malarious localities, the two others are comparatively rare.

The distinguishing points of the adults of this genus are the buccal appendages and the wings, and the position they assume when at rest.

From the head projects a long proboscis and two palpi, the latter being of the same length as the proboscis in both the male and female.

Upon the wings of the Anopheles claviger are four black spots arranged in the form of a capital T.

The Anopheles superpictus has four black spots arranged in line along the anterior or external edge of its wings, with intervening spots of yellow.

On the wings of the Anopheles pseudopictus the black spots are not distinctly marked, while the yellow spots are the same as in the former variety.

The Anopheles bifurcatus has no black spots upon its wings.

HABITAT. Mosquitoes live and thrive in low, moist localities, marsh lands, and the low lands covered with underbrush adjoining damp and dark woods, caves, stalls, etc., form their resting-place by day, whence they issue forth in the early evening, and inflict themselves upon man and animals.

As well as an aerial existence, mosquitoes have one in water; that is, the females deposit their eggs upon the surface of the water, where they develop first into larvæ, then into nymphæ, and, finally, the complete aerial insect is set forth.

This process involves from twenty-four to thirty-two days. The eggs of the Anopheles claviger, about forty to one hundred in number, are deposited upon the surface of the water in the form of a ribbon-like band, those of the Anopheles bifurcatus in a stellate formation; the waters preferred are stagnant, or semistagnant and clear; slow running ditches and canals, meadows, and rice fields are favorite places.

In about three days the larvæ are hatched; these have small heads and a short breathing-tube, and lie parallel to and just beneath the surface of the water, the breathing-tube and a portion of the head protruding above it. They feed in this position, and it is only late in the larval stage that they descend to the bottom for food, and this is done with great difficulty.

COMPARISON OF ANOPHELES AND CULEX.

Anopheles.	*Culex.*
Selection of water upon which to lay eggs:	Selection of water upon which to lay eggs:
Clear, quiet, slow running streams.	Artificial pools, receptacles in which water is left standing, grassy streams.
Larvæ: Head small and breathing-tube short.	Larvæ: Head large and breathing-tube long.
Do not descend to bottom until late in larval stage.	Feed on the bottom, ascending to the surface to breathe.
Larvæ lie just below and parallel to the surface, with breathing-tube and portion of head protruding above it.	Larvæ, while breathing, assume a position of 45° to the surface, breathing-tube protruding.
Adult mosquito:	Adult mosquito:
Palpi of both male and female the same length as the proboscis.	Palpi of female much shorter than the proboscis.
Certain arrangements of spots upon the wings.	No spots upon the wings.
When clinging to horizontal surfaces, the body is almost at right angles to the surface.	When clinging to horizontal surfaces, the body is parallel to the surface.
Vertical surfaces, body at an angle of about 35°.	Vertical surfaces, body parallel.

Malarial infection does not extend far in any direction from given foci, being limited in horizontal, oblique, and vertical directions; this is readily explained by the life of the mosquito.

I cite the following conclusions reached by Celli:

1. The hours during which the malarial germs are most plentiful in the air are those of evening, sunset, and night.

2. They generally rise from limited foci, and are diffused to a limited distance in the horizontal, oblique, and vertical directions.

3. The winds, properly called, do not generally transport them; they tend rather to diminish their number in the atmosphere.

4. Woods, instead of filtering them, may be foci of malarial infection.

These axioms are thoroughly in accordance with the theory that the malarial germ is cultivated, transported, and inoculated by the agency of mosquitoes, which—

1. By day lie hidden and sheltered, while they come out to bite man in the evening and at night.

2. They do not wander far from the place where they are born, and especially they fly a little distance from the ground.

3. When the wind blows they do not, as a rule, come out of their hiding-places.

4. Shady and damp woods and trees in general are the nests of mosquitoes. The mosquito, besides being the source, is consequently also the carrier of malarial infection.

Prophylaxis. With the foregoing facts in view, it is obvious that two courses of action present themselves: first the destruction of the mosquito, and, second, the prevention of infection spreading to non-infected mosquitoes; both of these being of extreme importance, not only to the individual or to the community, but to the State as well.

For as the efficiency of a body of troops in the field is directly proportionate to the health of the command, so is the prosperity and happiness of a State dependent upon the health of its inhabitants.

Therefore, from an economic standpoint, as well as from that of the public health, the State should make every effort to free itself from this most persistent and dangerous pest.

What applies to the State applies with even greater force to the community, for the municipality being so much closer to the individual can, by a process of education, and the passage of proper laws, and a rigid enforcement of them, practically destroy the mosquitoes, bringing health and prosperity where formerly quite the reverse was the case. Witness the city of Havana, Cuba, under the able administration of Major Gorgas, Medical Corps, United States Army, Chief Sanitary Officer, and upon a smaller scale the town of Winchester, Virginia, under the wise and progressive administration of its Mayor, Mr. R. T. Barton.

The part of the individual grows more important as the population grows more scattered, and in the smaller towns and isolated places of residence, it will be the work of the individual that will have to be depended upon for results; but in the larger towns and cities much may be accomplished by the intelligent co-operation of the individual with the proper authorities.

Duties of the State. The State, through the channels of its Board of Health, or a body with similar authority, should publish a health bulletin, or a mosquito bulletin, setting forth in a plain, concise manner the relation mosquitoes bear to disease, and also the economic side of the question, showing the relative rise in value of real estate, and the increase in productiveness of lands, which by proper drainage, etc., can be reclaimed, and made not only productive but habitable, thereby producing a great advantage to the individual, as well as to the community at large, and indirectly increasing the wealth and prosperity of the State. Copies of these bulletins should be sent to all local Boards of Health and Boards of Trade, and active co-operation urged and solicited; where extensive swamp lands are a menace to a community and State, the State should render financial help in the reclaiming of such lands.

Copies of these bulletins, with printed instructions as to the best and most improved methods of destroying the mosquito and its breeding-places, should also be sent to all State institutions, with orders to those in charge, that every precaution should be observed for the destruction of mosquitoes and their breeding-places, and inspections made from time to time, by competent inspectors, to see that the orders have been intelligently carried out.

Duties of the Municipality. Similar bulletins should be published by all local Boards of Health, and the individuals of the community thoroughly posted as to the necessity and the methods to be employed for the destruction of the mosquito; also the necessity of protecting all cases of malaria from the bite of mosquitoes, so that non-infected insects will not become infected, thereby spreading the disease.

The following sanitary measures should be adopted and put in force:

1. All hollows within the city limits, and for a mile surrounding it, should be filled in and graded.

2. Marsh lands within the same territory should be properly drained, and, where practicable, filled in.

3. Ponds and streams that cannot be drained or filled in should have their surfaces covered with petroleum, which should be renewed every twenty-one days.

4. Where for any reason this is impossible, fish should be introduced, so that they may feed upon the larvæ.

5. All receptacles holding water should be made mosquito-proof, or where this is impossible the surface covered with petroleum. If this water be drawn, by means of a faucet, from the botton of the cask or tank, and not dipped out, it will not be unfitted for drinking or washing purposes.

6. Old cans and pans exposed so that they might collect rain-water should be carefully covered.

7. Householders should be advised to thoroughly screen their houses.

8. Thoroughly screened isolation wards should be provided in the hospitals.

9. All cases of malarial fever should be reported to the Board of Health, the same as other infectious and contagious diseases.

10. Where the patient cannot be properly isolated at home, he should be removed to the hospital.

11. The sick room should be thoroughly screened, completely isolating it from the other portions of the house, as well as from the outside.

12. The mosquitoes in the other rooms should be carefully destroyed.

13. When the plasmodium has disappeared from the blood, the patient should be removed to another room, and the mosquitoes in the sick room destroyed by fumigation.

14. Cesspools should have their surfaces covered with petroleum at least once a week.

Duties of the Individual. He should make himself thoroughly acquainted with the mosquito question, and do everything in his power to aid the authorities in their efforts to destroy them and to protect himself and family from infection.

He should thoroughly screen his house, fill in and grade all hollows on his property, see that all receptacles in which water is allowed to collect and stand are mosquito-proof, or that the water surfaces are covered with petroleum.

If living in the tropics, or in a malarious locality, he and his family should wear warm underclothing, woollens preferred; they should remain indoors as far as possible after nightfall, or if compelled to go out, to protect exposed parts by netting or by the use of such drugs as are known to repel the mosquitoes. Tonic doses of quinine or arsenic are of great value to those habitually exposed to infection.

Methods for Destroying Mosquitoes. This subject has been given considerable attention by investigators all over the world, and various substances have been suggested for use in or upon waters infested by larvæ, as well as for the destruction of adult mosquitoes.

Among the substances suggested as larvicides are the aniline dyes, permanganate of potassium, and petroleum; the latter has been proven to be the only practicable substance of the many named, and is very effective.

The grade of oil selected for the purpose should not be too heavy or it will not spread properly over the surface, nor should it be of such quality as to evaporate quickly; the "fuel oil" of the Standard Oil Company seems to give the most satisfactory results.

An ounce of oil to every fifteen square feet of surface should be used.

Where, for any reason, oil cannot be used, small fish, such as minnows or sun-fish, should be introduced, as these feed upon the larvæ.

In the destruction of the adult mosquito, rooms should be carefully sealed, and such insecticides as sulphur, pyrethrum powder, or formalin used.

Major Gorgas, in Havana, found that pyrethrum powder proved the most satisfactory agent, as it was less offensive to the household, did not destroy or injure fabrics, and was very effective.

One pound of the powder to every 1000 cubic feet of air space should be used; as this does not entirely kill all the mosquitoes, but at times only stupefies them, causing them to fall to the floor, at the end of three hours the room should be opened, and the mosquitoes swept up from the floor and burned.

Drugs, which when applied to exposed surfaces, such as the face, neck, and hands, sometimes prove useful; the best of these are the oils of citronella, lavender, eucalyptus, and pennyroyal; camphor-water is also valuable.

THE THEORY OF CROSS EDUCATION AS APPLIED TO THE AUDITORY APPARATUS.

SOME EXPERIMENTAL STUDIES.

By Lewis S. Somers, M.D.,
of Philadelphia.

As long ago as 1836 the sympathetic relation of one ear with the other was recognized by Kramer, and since then varied physiological and pathological phenomena have directed the attention of careful observers to the apparent relation in functionating power exercised by one ear, upon the opposite side. As directly evident that such a phenomena exists, one has but to place a vibrating tuning-fork before one ear, and in the majority of instances the acuity of hearing in the opposite ear for a different sound, such as that of a watch, will be somewhat augmented.

In the so-called sclerotic or catarrhal otitis media, in which a trophic element undoubtedly plays an essential part, and in cases in which the hearing has been reduced in one ear to contact for the watch, a transient auditory stimulation may be produced by the sound-waves from a vibrating body, such as a Cii tuning-fork when placed near the

opposite ear, so that for a short time the hearing in what we may designate as the watch-ear will be increased, so that the high-pitched note of the watch will be heard at a variable distance, rarely exceeding, however, half of an inch. This gain in hearing apparently disappears when the sounding body is removed from in front of the meatus of the opposite side, but if the vibrations are allowed to continue for several minutes the hearing distance for the watch is diminished to the original contact, while from fatigue the hearing for the tuning-fork is also lessened. An analogous phenomenon is occasionally elicited under the same conditions in those cases where the watch is not heard on contact or is heard but faintly; the effect of the vibrating body of a dissimilar sound placed before the meatus of the opposite ear causing the patient to hear the watch when before such was not the case. The effect of the electric current when used to demonstrate this relationship between the two ears is not so well marked as the effects produced by sonorous bodies, but in some cases the electric stimulation of the auditory nerve of one side increases the susceptibility of the opposite nerve to the action of the current, while very infrequently under the same conditions the so-called paradoxical reaction may be elicited; this phenomenon consisting of obtaining the galvanic reaction in the ear to which the electrodes are applied, and at the same time there occurs an opposite result in the non-stimulated ear.

With the knowledge that such a relation existed between the two organs of hearing, and the apparent influence exerted one upon the other being capable of demonstration, it was but a step to apply the theory of "cross education," as enunciated by Scripture, to the aural apparatus in an endeavor to ascertain, as far as possible, the apparent cause of the relation existing between the two ears and which was concerned in the production of the phenomena previously described. Scripture's experiment consisted in squeezing the bulb of a mercury dynamometer as hard as possible with the left hand for a number of times, and the rise thus produced of the column of mercury was averaged. Immediately afterward the same process was performed with the right hand. Then on the following days, with some intermissions, the experimenter practised the right hand by squeezing ten times on each occasion. On the ninth and final day of the experiment the left hand, which had not received any practise in the interval, was again tested, and it was found that it had gained about 50 per cent. in strength through practise of the right hand. In other words, the original test on the first day showed on the dynamometer an average of 28.8 inches for the right, and 29.6 inches for the left hand, while during the course of the experiment from the exercise of the right hand the height to which the column of mercury could be raised gradually increased at each trial until the last day, when it reached an average of 48.6 inches. It

should be remembered, however, that during this time the left hand was not used at all for this purpose, yet at the termination of the experiment the increased strength in this hand had risen to 42.3 inches, as shown by the dynamometer. The peculiar phenomena thus produced of the transference of the effects of practise from one side to the other was called by Scripture "cross education."

To further demonstrate this another experiment was performed by trying to insert the point of a needle at the end of a rod into a small hole without touching the sides. At first twenty trials were made with the left hand, with a success of 50 per cent., and then the right hand was used in the same manner, with a success of 60 per cent. On succeeding days two hundred experiments were made with the right hand, with a final success of 88 per cent. Again the experiment was tried with the left hand, which had not been practised in the meanwhile, and a success of 76 per cent. was obtained, thus again demonstrating the results obtained from the original experiment. As corroborative evidence of the fact that cross education does exist, the experiments of Davis have a direct value, and, even further, they present features applicable to the synergy existing between the tensor tympani muscles of the corresponding ears. "The subject of this experiment began by raising a five-pound dumb-bell by flexing the arm at the elbow, this calling into play chiefly the biceps muscle for lifting and the forearm muscles for grasping. This was done as many times as possible with the right arm, and then, after a rest, with the left arm. The subject then entered upon a practise extending from two to four weeks, which consisted in lifting the weight with the right arm only. At the end both arms were tested as at the start." The results obtained from this experiment were exceedingly interesting, as, after careful measurements were made of the upper arm and forearm on both sides, it was found that the unpractised left arm had gained in power, as shown by the former experiments, and, in addition, it had also gained in size. As pertinent to the further elucidation of this subject, it is well to note here that Scripture considers the gain by practise, which shows itself by cross education, to consist in the development of the higher nerve centres connected with the two sides of the body.

With the results obtained by Scripture upon symmetrical parts of the body clearly established, and the knowledge of the so-called sympathetic relation existing between the two organs of hearing, I undertook to make a series of experiments upon the auditory apparatus to determine, if possible, what effect mechanical movements of the membrana tympani and, therefore, of the chain of ossicles would have upon the hearing power of the opposite ear. The cases selected for this purpose were those in which the hearing was defective from sclerotic changes in the conducting apparatus, but in which the percep-

tive portions were, as far as ascertainable by recognized auditory tests, not involved in the essentially chronic process. The method used in determining the effect of exercise of one ear upon the opposite one was to make the usual tests of hearing of both ears, the voice, watch, and tuning-fork being used for this purpose. Immediately thereafter movements of the membrana tympani and ossicular chain were made by rarefying and condensing the column of air in the external auditory canal by means of a ten-ounce Politzer bag and a Siegle otoscope tightly fitted, by means of a soft rubber tip, into the canal. The air in the canal was alternately rarefied and condensed for fifteen distinct times in the right ear, the pressure exerted upon the drum when the bag was forcibly compressed being sufficient to produce visible and well-marked to-and-fro excursions of the tympanic membrane, but not being forcible enough to cause any harm.

In order to eliminate as far as possible any extraneous sound waves, and especially the high-pitched sound caused by the escape of air between the wall of the external canal and the otoscope, special care was taken to have the ear-piece tightly in apposition with the canal wall, so that the production of any sound waves from this source could be entirely eliminated. These seances consisted of fifteen massage movements each of the drum and ossicles, repeated on the right ear on alternate days for ten times, and at the conclusion of the tenth seance the left ear was again tested, to ascertain if any change had occurred in the interval during which it had had no exercise. The results clearly demonstrated the phenomena of cross education, as shown by the following cases which were selected from a number performed, all with positive results.

The first experiment was performed on Mrs. L. A., aged thirty-eight years, who had complained of impaired hearing for one year. The membrana tympani were retracted and thickened on both sides; the Eustachian tubes were patulous, and she complained of tinnitus approaching a musical note. The Cii tuning-fork (512 vibrations) was used in testing, and Rinne was positive for both ears; Weber being positive for the left. The voice was only heard when loudly elevated for both ears, and the watch showed 0/54 for the right and c/54 for the left on the first day of the experiment, the "0" being equivalent to no watch hearing, while "c" meant that it was heard on contact only. The following table shows the result of the exercise and its effect upon the non-exercised ear:

	1st day	2d day	3d day	4th day	5th day	6th day	7th day	8th day	9th day	10th d'y
Right,	0/54	0/54	0/54	1/54	1½/54	¾/54	c/54	c/54	0/54	3/54
Left,	c/54	.....	.....	.....	.....	.....	.....	.....	.....	2¼/54

Thus, in the right ear the hearing increased from nothing for the watch to a fair hearing distance of 3 inches, while in the left non-exercised ear the hearing for the watch, which was originally only on contact, had increased to 2½ inches, a most remarkable gain and one which clearly demonstrates the effects of cross education upon the auditory apparatus. In this case both Rinne and Weber tests remained the same after the experiment was concluded, but the gain in hearing for the voice was shown in both ears, and instead of a loud voice being necessary in order to make the patient understand, a slightly elevated voice only was necessary even in the left ear.

Another case upon which the experiment was performed, and which will be sufficient for illustration here, is that of O. K., male, aged fifty years, with impaired hearing and tinnitus for four years. The membrana tympani presented the appearances seen in the former subject, but to a more marked degree; Rinne was positive in both ears; Weber positive in the right; the watch was heard in both ears only on contact, while a moderate voice could be readily understood. The diagnosis of chronic otitis media was made, without marked changes of the internal ear or auditory nerves. The same procedures were adopted as in the preceding instance, with the following results, not so well marked, however, as in the former case, but of sufficient import to be of value:

	1st day	2d day	3d day	4th day	5th day	6th day	7th day	8th day	9th day	10th d'y
Right,	c/54	c/54	½/54	3/54	3/54	3¼/54	c/54	2½/54	3½/54	c/54
Left,	c/54	.....	.....	.....	.....	.....	.....	.....	.....	1/54

In this instance a gain of 1 inch in the left unpractised ear was obtained by the stimulation alone of the opposite organ of hearing. Rinne's test remained, like that of the voice, unchanged, while Weber's now became positive for both ears.

It will be noticed in both individuals that in the exercised right ear there were, from time to time, considerable variations in the hearing distance. These retrogressions are well marked in all cases of aural sclerosis, and may be the result of numerous extraneous causes, and in the particular cases under observation the temporary diminution in the auditory capacity was the result of two distinct causes, one being a temporary closure of the Eustachian tube from a transitory rhinopharyngitis, while the second factor was undoubtedly the result of overstimulation of the receptive portions of the auditory apparatus, with a subsequent transient fatigue and diminution of response to the usual stimuli. This factor was easily demonstrated by omitting the massage movements for a day, when the hearing capacity would again assume its acuity previously gained.

Another factor which was noted during the course of these experiments, and which also presents some features of practical import, was the effect of the passive movements of the right ear upon the tinnitus which existed in the left ear. In the first instance the subjective sounds were quite distressing in both ears previous to the tests, while after their completion the tinnitus appeared to be much better in the right ear, while on the opposite non-exercised side the improvement was marked, but not to the same extent. In the second case, however, in which the tinnitus resembled the sound produced by escaping steam, and while present in both ears, was worse in the left; yet as the result of the massage it slightly diminished in the right and improved to a considerable extent in the left ear. The phenomena observed in these and other cases of the effects of cross education were not only confined to an increase in the functional activity of the passive ear, but also influenced the pathogenic factors present to some slight extent, as shown by the partial subsidence of the tinnitus.

As but a minimum of direct sound is produced by the massage movements as employed under these circumstances, the influence exerted upon the auditory nerve and receptive centres is mainly that of mechanical stimulation, being obtained by the to-and-fro movement of the column of air in the external auditory canal and Politzer bag employed for this purpose against the more or less resisting drum membrane. The effect of this rarefaction and condensation of air being to alternately move the drum backward and forward and in turn producing a transmission of this energy through the ossicular chain to the perilymph in contact with the inner aspect of the oval window; the impulses so produced were transmitted through the natural paths of the internal ear to the delicate terminations of the auditory nerve, and thus acting as more clearly defined sound waves of measurable length.

That the stimulation so produced assumes a mechanical feature, more than a pure auditory aspect, I believe to be the correct interpretation, and that this is evident is well shown by some of the phenomena elicited in the study of the physiology of the auditory nerve and its end organs. It is a well-known physiological fact that the eighth nerve is capable of conveying other impulses than those purely of audition, and the presence of motor fibres here, as well as those of a sensory character, will admit of the transmission of impulses not especially concerned with audition. This is especially seen in the studies of the peripheral distribution of this nerve to the ampullæ of the semicircular canals, where the fibres partake essentially of motor activity, while those filaments which are distributed to the other portions of the labyrinth are sensory in their function. By direct experimental stimulation of the ampullar terminals it is possible to excite reflex motor activities, which are conveyed to the higher centres through the nerve trunk, and exercise

undoubtedly some control over equilibrium. This is especially prominent when non-auditory massage movements are applied for various reasons to the membrana tympani, for should the force be too powerful, an over-stimulation of these motor fibres in the ampullæ ensues and greater or lesser degrees of vertigo immediately occur.

The auditory nerve in whatever form the motion may originate from is excited by the mechanical stimulation of the wave motions of the labyrinthine fluids. And while it is not desired here to enter into the complex aspects of audition from this point of view, it may be noted, in order to more clearly indicate the nature of this aspect of cross education, that the fluid of the internal ear is moved apparently as a whole and not in molecular parts. In addition, it seems very probable, and to my mind, at least, conclusive, that the various forms of motion, whether concerned in pure audition or in other mechanical stimulation, are conveyed to the fibrillary terminations of the nerve, not only through the ossicular chain and oval window, but also by the movements of the air waves in the tympanic chamber, through the inner tympanic wall and fenestra rotundum, thus producing movements of the contained fluid by these dissociated routes. The action of these massage movements as used for therapeutic purposes, but which well apply to our subject here, were studied by Nuvali, who found in the dead body that by making apertures in the roof or sides of the tympanum the intratympanic structures might be observed while massage movements were performed. The vibratory motion of the intralabyrinthine fluid being ascertained by observing the movements of the membrane in the fenestra ovalis, it was also found by drilling a minute aperture into one of the semicircular canals that the fluid filling it also partook of the same vibratory motion.

An interesting hypothesis advanced by Gad in relation to the functions of the eighth nerve is also of interest in a study of cross education, as he considers that this nerve trunk not only transmits stimuli resulting from the analysis of complex sounds by the labyrinth, but it is also excited by the impulses of the vibrating body acting as a mechanical stimulus. As to the receptive centres with which the eighth nerve is in affiliation as regards the perception of the stimuli with which we are concerned other than those of purely acoustic origin, little can be said, except that they, undoubtedly like other centres, react to other stimuli than those for which they were especially designated, although, of course, certain centres are immediately concerned in the control of the sum total of those stimuli (some motor) which go to make up what we call equilibrium.

The anatomical relation of one auditory nerve to the other seems to show in a manner the relation existing between the two ears, and their synergy evidently is dependent to some extent upon these close relations.

An examination of the auditory nerves at their origin shows that a portion of their fibres is closely connected with a mass of motor cells in the bulb, and that these fibres pass into and are continued in the inferior peduncles of the cerebellum. Further than this there is a decussation of the fibres in the region of the trapezoid bodies, and this certainly suggests some correlation of auditory impressions or other stimulation in the higher centres of the two symmetrical organs. And this anatomical feature seems still more to be indicative of these cross educational features when it is considered that each nerve communicates with both centres, and that each contains a decussating and a smaller non-decussating fasciculus.

The influence of the auditory functions of one side upon that of the other in a retrogressive and passive sense, instead of active motion which has been dwelt upon, is illustrated in a case coming under the observation of Ouspenski, and which well shows this reciprocal influence. The case was one of acute unilateral otitis, in which there existed bilateral deafness. Examination showed the presence of a piece of wool in the inflamed ear, pressing tightly upon the membrana tympani, and when this was removed the hearing returned to normal in both ears. This same influence has been repeatedly noted in the opposite ear when one or more ossicles have been removed from but one tympanum only.

Similar to this are the results seen in those cases of sclerotic otitis media in which one or more ossicles have been removed. This beneficial influence upon the non-operated ear has been especially noted by Burnett, and as a result of his extensive experience with this operation he found that the results indicate that the progressive impairment of hearing, while being stopped in the ear operated upon by the removal of the incus, was similarly influenced in the opposite ear; and a case under his observation for six years showed this correlation in a most striking manner. Dench has also called attention to the improvement of the function of the non-operated ear, while in a case of progressive deafness seen by Alderton, in which he removed the incus and crura of the stapes, and later trephined the foot-plate of the stapes, it seemed to arrest the progress of the deafness in the ear operated on and improved considerably the hearing in the opposite ear not operated on, the result in the opposite ear being due to what was considered the synergy of the two sides. Miat has also noted this phenomena, and states that when in a patient affected with dry otitis the worse ear alone is operated on, the increase in auditory acuity is noted not only on the operated side, but also in the other ear, especially by submitting it to some form of electric stimulus. Under such conditions the correlation between the affected ears assumes a practical import, and while it would not be judicious to take into consideration improvement in the non-operated

ear as a part of the prognostic features of a case, yet this beneficial result has been noted by so many observers that it is worthy of more careful study.

As the study of cross education is best made in those cases where the auditory acuity has been somewhat dulled by sclerotic processes, so may the course of this morbid process strikingly suggest the interdependence of the organs of hearing. For the disease usually begins in but one ear, while the opposite cavum tympani remains apparently unaltered for a considerable time, and then later becomes involved much more rapidly than the originally affected ear. This effect is certainly not seen in non-correlated areas of the body under the same existing conditions. Various observers have noted the effect on increased labyrinthine tension from rigidity and displacement inward of the ossicular chain upon the function of the opposite ear, while Urbantschitsch urges that stimulation of the perceptive centres may follow the action of sonorous vibrations, even if the ear acted upon is so defective as to be incapable of transmitting impulses to the degree necessary for actual sound-perception on the part of the patient, and he considers that when the ear of one side has been rendered entirely useless by sclerotic changes in the conducting mechanism it is warrantable to relieve this abnormality before the influence which it may exert upon the opposite side can be decided.

As regards the correlation between the corresponding portions of the auditory apparatus on the opposite sides, various theories have been suggested to account for the phenomena, especially in pathological states. Dench considers that the relationship no doubt depends upon reflex action through the sympathetic and cranial nerves, and in many cases upon the decussation of the auditory fibres within the brain. Rhese, in considering the improvement following in the opposite ear after removal of the ossicles in two cases which came under his observation, states that it is probable that the removal of the malleus destroys the synergic action of the tensor tympani muscle in the opposite side, and thus accounts for the improved hearing and arrest of the subjective noises. Another theory which he considers is that by the anastomosis of the auditory nerves one with the other, inhibitory stimuli are transmitted through the tympanic plexus to the sound-perceiving part of the other ear, and Burnett offers as an explanation of the improvement in the opposite ear that the contraction of the tensor tympani being overcome by the removal of the incus in one ear, the synergetic contraction of the tensor in the opposite ear, induced by cross influence of the more diseased organ, was also overcome by a beneficial cross influence emanating from the operation in the diseased ear.

That the phenomena of cross education as related to the auditory

apparatus can be readily demonstrated, I am confident admits of no doubt, and that the correlation existing between the auditory apparatus of the opposite sides of the body is that of so-called cross education, seems probable in the light of my experiments. The relation of the fibres of one auditory nerve with that of the other and with the higher centres in intimate relation with the nerves from both sides evidently, in part, at least, indicates the paths by which stimuli applied to one side in turn influence the other correlated area.

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A CASE OF ACUTE LYMPHATIC LEUKÆMIA WITHOUT ENLARGEMENT OF THE LYMPH GLANDS.[1]

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THE different forms of leukæmia, and especially the etiology of the disease, have formed a subject of great interest to the medical profession since Virchow's first publication in 1845. When we attempt to review the colossal amount of literature on this subject, in the endeavor to learn what has been discovered and to trace the genesis of the prevailing opinions, we are surprised to find how little is definitely known concerning the nature of the disease and how much remains to be elucidated.

The excellent papers of Müller[2] and Walz,[3] which almost completely cover the literature, greatly facilitate the review of the facts and opinions relating to various branches of the subject. I have depended largely on the article of Walz for the summary of the existing knowledge of the subject, and more particularly for references to the form of the disease to be considered in this paper.

The scope of this paper is to present some suggestive points which a study of a recent case of acute leukæmia has offered. The clinical

[1] From the Pathological Laboratory of the Johns Hopkins University and Hospital.
[2] Centralbl. f. allg. Path. u. path. Anat., 1894, Bd. v. pp. 553, 601.
[3] Ibid., 1901, Bd. xii. p. 967.

features, the autopsy report, and the microscopical findings of the case will be briefly presented.

Clinical History. Mr. C., a patient of Dr. Smart's, Baltimore, Md., to whom we are indebted for the notes of the case. Born in England, forty-seven years ago. A gardener by occupation. Always a very healthy man. Florid complexion. Digestion good. Heavy drinker. Denies venereal diseases. Fifteen years before had a protracted attack of malaria.

Six months before his death had a severe hemorrhage from the nose. From this time on became noticeably pale.

Called in a physician, three and a half weeks before his death, after having a second hemorrhage from the nose. His chief complaint was dyspnœa and great weakness. The change in complexion was startling, his pallor being extreme and increasing progressively up to the time of death. Over his left fibula there was a small area of subcutaneous hemorrhage. A hæmic murmur was heard over the præcordium. There was no fever, cough, or pain, or any other pronounced symptoms. The asthenia progressed. The urine appeared normal, except for an excess of uric acid.

The blood was examined twice microscopically, ten days and seven days before death. An enormous increase in the leucocytes was apparent, the white cells being about as numerous as the red blood corpuscles. No differential count or more accurate examination was made.

Four hours before death, some altered blood was expectorated, which presumably came from the nose and was swallowed.

The patient died at 2 A.M., March 15, 1902.

Autopsy by Dr. W. G. MacCallum six hours after death.

Anatomical Diagnosis. Lymphatic leukæmia. Bronchopneumonia. Œdema of lungs.

Body is that of a fairly well-built man of moderate size. The skin is extremely pale.

Peritoneal and pericardial cavities appear normal.

Thorax. The pleural cavities are almost free from adhesions, only a few being present over the apices of the lungs, where there are depressed scars on the surface of the lungs.

Heart. Over the epicardium are a few small hemorrhages, especially over the right ventricle. Upon opening the heart it is found that very little blood can be squeezed from it. The cavities are filled with a whitish chicken-fat clot in which there is only a little red color noticed in the more dependent parts. The clot is quite continuous and may be turned out as a mould. The tricuspid and pulmonary valves are normal. The mitral and aortic valves are also normal, although they are slightly thickened. The myocardium of the heart is very soft and flabby, and everywhere shows an extreme mottling with yellow patches, which stand out prominently in contrast to the pale brown of the heart muscle itself. On tangential section, this mottling is extremely well marked, especially in the papillary muscle, where it has the typical faded-leaf appearance. The anterior descending branch of the coronary artery shows quite marked patches of sclerosis. There is also a little sclerosis in the root of the aorta. There are no thrombi, and the endocardium is everywhere smooth.

Aorta. The aorta contains but very little blood, and that is coagulated into blood clots. The walls of the aorta are fairly normal.

Lungs. On removing the lungs the pleural surfaces are found to be smooth and glistening. The lungs are very voluminous and pale. Over the apices are found areas which are collapsed. On section the lung substance is found to be a little emphysematous, especially in the upper portions; they are extremely œdematous throughout. Only in the collapsed portions near the apices is there any evidence of consolidation, and here there are one or two small bronchopneumonic patches. The bronchial glands are deeply pigmented and only moderately enlarged.

Both lungs present practically the same appearance. The trachea is very pale, but apparently normal.

Spleen. Measures 13 x 10 x 6 cm. The surface is quite densely adherent to the diaphragm at one point. There is some thickening of the capsule and a few small hemorrhages show through. The vessels at the hilum are not especially thickened. The organ is firm in consistence, and on section the pulp is somewhat translucent, grayish-red in color. The Malpighian bodies are visible and are somewhat diffuse; they are not sharply outlined, although they differ very markedly from the red splenic pulp. The trabeculæ and vessels are moderately prominent.

Liver. Measures 25 x 18 x 9 cm., and extends 10 cm. below the ensiform cartilage. The surface is smooth and the lobulation is normal. The cut surface is pale brown in color, and there are many lobules with bright-red centres. There are some small, pin-head-sized areas which are translucent gray in appearance, and seem to be situated about the vessels. On the whole the liver substance has a normal appearance. The lobules are indistinctly marked out and the consistency of the organ is not increased.

Œsophagus, stomach, and intestine, except for a marked pallor of the mucosa, appear normal. The lymph follicles are nowhere enlarged.

Kidneys. The organs are about alike in general appearance. The capsule strips off readily, leaving an extremely pale surface which is quite smooth. The left kidney measures 12 x 6 x 3.5 cm. The cortex averages 5 mm. in thickness. The cut surface is also extremely pale, pyramids being especially white. The cortex has a grayish color throughout. The striations are just made out and only here and there can a glomerulus be seen. Scattered over the surface of the cortex and pyramids are opaque yellow-white specks of minute size, which are more abundant in the pyramids. The pelvis and ureters are apparently normal. Adrenals are normal in appearance. Bladder also apparently normal.

Lymph Glands. The bronchial and all the peritrachial and aortic glands, though deeply pigmented, are not especially enlarged and are rather soft and translucent. The mesenteric lymph glands are also not enlarged, are deeply pigmented, grayish-yellow, and translucent, and on section somewhat softer than normal. They are quite closely crowded in the mesentery. The inguinal lymph glands are not especially enlarged and are rather pale and soft, like those described in the mesentery. Along the retroperitoneal region the hæmolymph glands are very conspicuous, have a dull-red color, and are not especially enlarged.

Thoracic Duct. The thoracic duct is found not enlarged and contains a slightly blood-stained fluid.

Bone Marrow. The bone marrow of the femur is homogeneous, deep red in color and very soft and diffluent.

Microscopic Examination. Blood. At the autopsy blood smears were made from the heart and vena cava. The films were fixed by heating on the copper bar. The best nuclear differentiation was obtained by following Rubinstein's method of heating from thirty seconds to one minute at the spheroidal point. Ehrlich's and Biondi-Heidenhain's triple stains were used, also dahlia, eosin, and methylene blue, polychrome methylene blue, safranin, etc. In making several differential counts of these preparations, in over a thousand non-granular mononuclear cells, only three or four granular leucocytes were seen, and these were polymorphonuclear. Four normoblasts were seen in the count.

The uninuclear cells varied in size from cells almost twice the size to those considerably smaller than the normal red blood cells. The nuclei were round or slightly oval. In the large cells, the nucleus stained faintly, and showed a definite nucleolus and intranuclear network. These chromatin threads took a red stain in Biondi-Heidenhain stain. The protoplasm of the cell was considerable in amount, non-granular and took a faint acid stain in eosin and methylene blue. The protoplasm of the cells, in specimens stained by a single alkaline stain, showed no basic granules and were only faintly tinted. Lymphoid cells with double nuclei and nuclei showing constrictions were occasionally found, but no mitotic figures were observed. The small uninuclear cells had only a slight rim of protoplasm, which also took preferably a faint acid stain. The nucleus stained intensely and usually homogeneously; however, a single point or chromatin filament, which retained a red stain in Biondi-Heidenhain's preparation, was to be made out in good specimens. It was impossible to make a definite estimate of the relative number of these two varieties of cells, as the fragmentation of nuclei and distortion of cells from post-mortem changes was considerable.

The red corpuscles appeared normal in size, form, and staining properties. The nucleated red cells were of the normoblastic type. The number of red cells present was remarkably small, but no estimation of the grade of anæmia could be made, as the blood was not fresh.

A chicken-fat clot from the heart showed on section a meshwork of fibrin containing the blood elements. This furnished a very clear picture of the different forms of leucocytes present. The predominating cell, as in the blood smears, was a small lymphoid cell, with a small round or oval, densely staining, homogeneous nucleus. The amount of protoplasm of such cells appears greater than in the blood smears, and although containing no definite granules, had an irregular granulated appearance. Similar cells, with a faintly staining nucleus, taking a greenish color in methylene-blue preparations, were considered to be degenerating cells, although the resemblance to normoblasts was striking. A few typical lymphocytes were seen, having a relatively large deeply staining nucleus, with a well-marked chromatin intranuclear network and a small rim of protoplasm. Larger cells, often over twice the size of a red blood cell, having a large vesicular nucleus, either pale or heavily stained, were more abundant than the typical lymphocyte. The nuclei of these cells, which were usually round but

occasionally slightly irregular in shape, showed always chromatin threads, and granules at the intersection of these filaments, and stained, as a rule, more faintly than those of the smaller cells. The protoplasm was often considerable in amount, and took a faint acid stain in eosin and methylene blue. No granulations were demonstrable in any of these lymphoid elements.

Lymphoid cells with two nuclei, or nuclei showing a marked constriction, were occasionally seen, both in the small and in the larger forms.

A few cells were observed with a relatively small vesicular nucleus, and a large amount of protoplasm containing blue granules in the alkaline stains. The ordinary polymorphonuclear neutrophile and eosinophile were rarely met with. No definite myelocytes or normoblasts were observed.

Bone Marrow. The study of the bone marrow of the femur showed an almost complete obliteration of the normal appearance of the bone marrow. This was due mainly to the disappearance of fat, and to the increase in the cellular elements, which were noticeably of a small mononuclear form. The tissue consisted of an almost homogeneous distribution of cells and red blood corpuscles in a network made up of very fine reticulum fibrils. The bloodvessels were apparently normal, the venous sinuses were, however, conspicuously large and full of cells. The capillaries could not be traced for any distance in the parenchyma, but seemed to break up and opened directly into the tissue spaces. The connective tissue present was very small in amount and was represented by an occasional cell, belonging to the reticulum, by the remaining fat cells, and the perivascular tissue. Stars of fibrin radiating between the cellular elements were abundant. The tissue was very congested, the vessels were not only full of blood, but red blood corpuscles were found lying everywhere in the tissue spaces, between the nucleated elements. In several areas definite hemorrhage had occurred, and the corpuscles were degenerated and coagulated together.

Very few nucleated red cells were to be made out, and these were of the normoblastic type. Practically no megaloblasts were seen.

Of the colorless cells present, the predominating cell was the small lymphoid cell, described previously in the blood. Here also it was conspicuous by its dense, deeply staining nucleus, of a round or oval shape. The next most numerous cell was the typical lymphocyte, with a nucleus showing a network of chromatin threads. Both these varieties of small lymphoid cells were found frequently dividing amitotically. The distinction between the appearance of the nuclei was maintained in the daughter cells. The two separating nuclei were always either dense and homogeneous, or slightly vesicular, and with a well-marked chromatin network. Practically no karyokinetic figures or signs of mitotic division were observed. The protoplasm of these cells stained faintly in acid stain and had a somewhat indefinite granular appearance. No definite granules were made out in any stain.

Very small cells, half the size of a red blood corpuscle, were fairly abundant in the bone marrow. These dwarf cells had a round, very faintly staining blue nucleus, and a small amount of homogeneous protoplasm taking a faint acid stain. The nature of these cells was not determined. The possibility of their being normoblasts was considered.

Large uninuclear cells, about the size of a myelocyte, with large, oval vesicular nuclei, were frequently seen full of basophilic granules. Large lymphoid cells with rather pale nuclei and non-granular protoplasm were present in large numbers. Cells with irregular or indented nuclei and non-granular protoplasm were also seen. The myelocytes present were relatively greatly reduced in number, but otherwise showed no change from the ordinary eosinophilic and neutrophilic varieties normally met with. The polymorphonuclear leucocytes were extremely few in number. A peculiar cell as large as a myelocyte, having a rather small, oval, densely staining nucleus, and a large amount of deeply staining pink protoplasm, was occasionally found. A few typical plasma cells were seen.

The giant cells of the bone marrow appeared diminished in number. Large phagocytic endothelial cells, containing often vacuoles, lymphoid cells, or red blood corpuscles were quite abundant.

Smears from the bone marrow furnished the same variety of forms as observed in the sections and showed in addition some important points. Transitions between the large lymphoid cell with the pale, vesicular nucleus and frequently basophilic protoplasm to the myelocytes with neutrophilic granules were evident. The nucleus of the older, more densely granular myelocytes showed more irregularity and stained more deeply. Nucleoli were conspicuous in the large lymphoid cells; and the nuclei of all the myelocytes and leucocytes, except the polymorphonuclear leucocytes, the nuclei of the small lymphoid elements showed in the triple stain red threads, which Rubinstein thought the distinguishing characteristic of the lymphoid cell of the bone marrow. These were more abundant and brighter in the ordinary sized lymphoid cell, but were still perceptible though faint in the large lymphoid cells, and in the myelocytes. We do not believe that these red nuclear threads are characteristic of bone-marrow cells, as the same thing can be demonstrated in cells of the lymph follicles and in the lymphocytes of the blood, contrary to Rubinstein's assertion. It is true that these markings are best seen in the young lymphoid cell and in the immature normoblast. The pyknotic nucleus of the mature normoblast loses this distinctive staining property, and the older lymphoid cells or marrow cells only show it faintly, while it is not evident in the polymorphonuclear leucocyte. This peculiarity would seem then to be a property of young cells, and the fact that the young normoblast, as well as the young lymphocyte shows it, speaks possibly for the common derivation of the erythroblast and the leucoblast.

The marrow of the rib showed a similar preponderance of lymphoid elements, as described in the transformed yellow marrow of the femur.

Lymph Glands. Lymph glands were examined from the axillary, inguinal, bronchial, retroperitoneal, and mesenteric regions. The condition was practically the same in every situation. The glands were not enlarged. The distinction between follicles and sinuses was partially obliterated from the increase of cells in the sinuses and to a lesser extent in the follicles. The structure of the tissue thus became more uniform and less characteristic of the lymph gland. The large cells, "mother cells" of the follicles, did not appear to be increased in number, nor were many mitotic figures to be seen in such cells. There was no evidence of proliferation in the gland itself. On examining with the high power the cells which were infiltrating the gland tissue, the great

majority of them appear to be very small lymphoid cells, of the type previously described in the blood and bone marrow. The small, deeply staining homogeneous nucleus was easily distinguished from the large, heavily marked nucleus of the gland lymphocyte. This was sufficiently distinct in ordinary preparations, but in eosin and polychrome methylene blue these cells showed a pale robin's egg blue nucleus in contrast with the deep indigo blue of the lymphocyte, and the contrast was easily made out with the low power. The bloodvessels were crowded with such cells, they filled the sinuses along with proliferating endothelial cells, and lay among the cells of the follicles to a less extent. In the capsule, groups of such cells were readily distinguished.

Larger lymphoid cells were found abundant in the sinuses, and presumably many of these also came from the bone marrow by way of the blood, as was evident in the case of the small cells. However, morphologically and in staining properties these larger lymphoid cells were identical with the cells of the lymph gland itself. No evidence of direct division in these lymphoid elements, derived from the blood was to be seen with the exception of a few irregular nuclei.

The mesenteric glands contained a large number of mastzellen, and quite numerous eosinophilic cells. Large cells containing brown pigment granules were numerous in glands near the pancreas and about the cœliac axis. A good-sized hæmolymph gland from the tissue back of the aorta showed no unusual appearance.

Spleen. The most marked changes in the spleen were the extreme congestion, and the increase of nucleated cells in the splenic pulp. This gave the tissue the appearance of an almost homogeneous structure, although the Malpighian bodies were still plainly visible. The capsule and trabeculæ were not thickened. The cells present in such great numbers throughout the splenic tissue were for the most part small mononuclear cells. They were scattered almost uniformly through the tissue. Red blood corpuscles filled the venous sinuses, and were found in great numbers in the intercellular spaces. Quite numerous nucleated red blood cells were observed, many of them showing signs of degeneration. In the Malpighian bodies there was no evidence of proliferation, either in the presence of mitotic figures or in the increase in the size of the follicles, as would be expected if the lymphoid cells present were to any extent of splenic origin. In sections stained in eosin and methylene blue, the majority of the infiltrating cells appeared similar to the small lymphoid cell described in the bone marrow, and were easily distinguished from the other large lymphoid elements present by the dense, small nucleus, and relatively large amount of protoplasm, and by the peculiar shade of light blue which the nucleus stained. There was no evidence that these cells were actively proliferating as in the bone marrow.

It was impossible to tell the origin of the other lymphoid elements present, as their morphology and staining properties were identical with the ordinary lymphocyte of the blood. Many of them doubtless came from the bone marrow, where similar cells were found greatly increased in numbers, and actively dividing.

Liver. The liver showed a varied appearance microscopically. The veins and liver capillaries were much distended and full of blood. The mononuclear elements in the blood were in such great numbers that the liver lobules were injected, as it were, with lymphoid elements.

There was also a marked infiltration about the portal spaces of small mononuclear cells. Some of these areas were of such size as to form small lymphomatous foci. The two types of lymphoid cells described in the blood and bone marrow were easily distinguished. The greater proportion of the cells were of the small lymphoid type, with the deeply staining homogeneous nucleus.

The parenchyma of the liver showed widespread degeneration. There was a general cloudy swelling of the liver cells. Small and large areas of cell necrosis were present. In the large necrotic foci the liver cells had disintegrated entirely and were unrecognizable. Hemorrhages into such areas were common. The capsule was not especially thickened, but showed considerable infiltration with lymphoid cells.

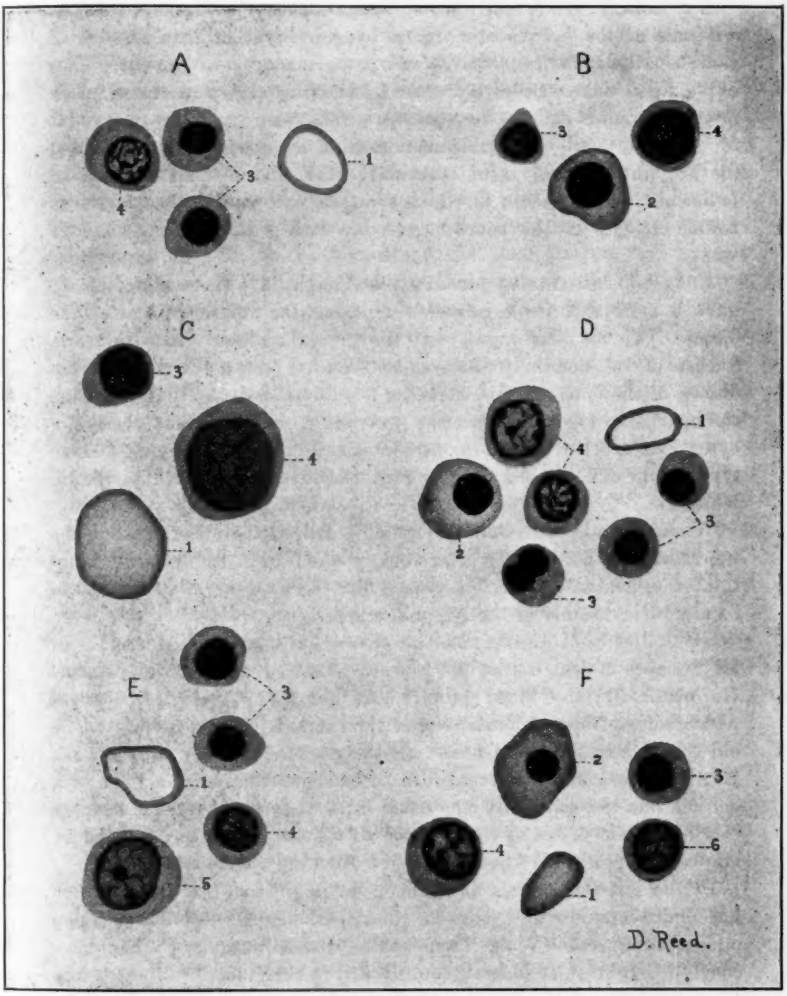
Lung. The sections of lung showed a marked œdema with a few areas in which the alveoli were filled with fibrin and red blood cells. The tissue everywhere was considerably congested. The bloodvessels, especially the veins, were distended with cells, among which small uninuclear lymphoid cells were the predominating form. Similar cells were also seen filling the capillaries and frequently in the alveoli. The pleura was delicate and not infiltrated to any extent by lymphoid elements.

Kidney. The cells of the kidney tubules were in a condition of acute parenchymatous degeneration. There was considerable congestion of the organ. Small foci of lymphoid cells in capillaries were visible through the tissue. No areas of lymphoid infiltration were seen. The capsule appeared normal, and there was no connective-tissue increase in the organ.

Heart. There was marked œdema and considerable fragmentation of the myocardium, otherwise the heart muscle seemed normal. The vessels contained as elsewhere a great number of lymphoid cells, but were not especially distended.

Muscle. The diaphragm and ileo-psoas muscles were examined, but without discovering any abnormal appearance other than the increase of the small mononuclear elements in the bloodvessels. The two different types of lymphoid cells spoken of repeatedly before were also easily distinguished here.

Before considering the details of this case, and its bearing on our knowledge of the nature of leukæmia, it may be well to review briefly the various opinions which have been held concerning this disease, and which, though widely divergent, have influenced our present conception of the subject. The early division of leukæmia, made by Virchow into the splenic and lymphatic forms, according as the spleen or lymph glands appeared to be the seat of the disease, is no longer in use. The enlargement of the spleen is not considered to be essential to the disease, and, indeed, there is much doubt if either of these organs is ever primarily involved. The idea that the origin of the disease lay in the hæmopoetic organs has prevailed since the publication of Virchow, in spite of considerable opposition from investigators who did not accept this view. Löwit's theory that leukæmia was a disease of the blood itself, the organs being only secondarily affected, has no longer any recognition.



Drawn with the camera lucida, Zeiss microscope, Oc. 4, Obj., oil immersion $^1/_{12}$.

Group A represents all types from section of a blood clot. Group B, cells from a blood smear. Group C, cells from a bone marrow smear. Group D, cells from a bone marrow section. Group E, cells from a lymph-gland section. Group F, cells from a spleen section.

Cell 1, normal red blood corpuscle. Cell 2, nucleated red blood corpuscle. Cell 3, small lymphoid cell, originating in bone marrow. Cell 4, lymphoid cell of bone marrow or lymphocyte of blood, and lymph gland. Cell 5, mother lymphoid cell of lymph gland. Cell 6, lymphoid cell of Malpighian follicle.

The similarity of the lymphoid cells from the different hæmopoetic organs is apparent. The nuclear framework of such cells is characteristic. The fact that the young normoblast has a nucleus in which chromatin threads can be demonstrated is shown in Group B, which was stained in the Biondi-Heidenhain mixture. The similarity between the normoblasts and the small lymphoid cells, which are in active proliferation in the bone marrow, is noticeable; the same chromatin threads are shown by the triple stain in the nuclei of these cells, which are usually so dense and homogeneous.

Neumann, in 1870, really strengthened Virchow's view that this was a disease of the hæmopoetic organs, by showing that in a number of cases a pathological condition of the bone marrow was present. This explanation cleared up several cases in which enlargement of the spleen or lymph glands had not been present or had been too slight to account for the symptoms. A myelogenous form of the disease was then added to the clinical divisions of leukæmia. His dictum that no case of leukæmia was on record in which a careful examination had failed to reveal changes in the bone marrow has had great influence on later work.

Ehrlich in introducing micro-chemical methods in the study of blood, gave a more definite means of diagnosing the different forms of the disease. To his teaching is due the prevailing view that leukæmia consists of two definitely distinct and separate forms, one arising from disease of the bone marrow, the other from disease of the lymph glands, the blood showing in one case the presence of great numbers of myelocytes, in the other an enormous increase in the lymphocytes. These types of the disease are known by the terms myelogenous and lymphatic leukæmia.

We might add here that to Ebstein's collection of the cases in the literature and to Fränkel's later work on the subject is due our conception of an acute form of leukæmia which is now generally supposed to be almost invariably of the lymphatic type.

The influence of Ehrlich and his school has been marked here, as in all diseases in which the blood changes are of especial importance. Unfortunately, the blood picture and not the pathological changes which caused these differences was emphasized in his teaching. The old school based their diagnosis on the organ especially enlarged, the Ehrlich school on the different form of leucocyte increased in the blood, neither one was especially concerned with the nature of the changes causing either of these conditions. Divisions of a disease based on clinical symptoms may be correct, but often only accidentally so.

In the last few years a new school, we might say, has arisen, which has endeavored to find out on what pathological foundation these clinical types rest. Walz,[1] Pappenheim,[2] Bradenburg,[3] and others have concluded from their investigations that the bone marrow in every case of leukæmia is the primary seat of the disease, and the origin of the cells which give the characteristic appearance to the blood. The other organs are only secondarily involved, in the general hyperplasia of lymph adenoid tissue which occurs. This is, of course, only a further development of the view set forth by Neumann, and rests on careful

[1] Arb. aus dem. path. Inst. Tübingen, 1899, Bd. ii. p. 1.
[2] Zeitschr. f. klin. Med., 1900, Bd. xxxix. p. 171.
[3] Charité Annalen, 1900, Bd. xxv. p. 85.

post-mortem examinations, and especially on the study of the bone marrow.

The important points in this case are that in a sudden and rapidly fatal illness, in which there were no especial features other than hemorrhage, anæmia, and a marked increasing weakness, there was present the blood picture of an intense lymphocytosis, establishing thereby the diagnosis of acute lymphatic leukæmia. At autopsy, as during life, there was no enlargement of either lymph glands or spleen, but the bone marrow showed macroscopically the features of lymphadenoid degeneration. Under the microscope, the bone marrow was found to consist mainly of lymphoid elements, the granular cells of the parenchyma being conspicuously few in number. These lymphoid elements consisted of two varieties of cells, one smaller than the red corpuscle with a densely staining homogeneous round nucleus and a small amount of clear protoplasm, the other, small and large cells of the typical lymphocytic type, the nucleus relatively large in respect to the protoplasm and showing always a nuclear framework. Both types of lymphoid cells were proliferating rapidly by direct division in the bone marrow. The blood was full of these elements, and all the organs examined were injected, as it were, by these lymphoid cells, which, however, showed no evidence of proliferation outside of the bone marrow. In the spleen and lymph glands the ordinary lymphoid cells of the lymphatic tissue could be easily distinguished from the small cells which had come from the bone marrow both by their morphological and by their staining properties. There was no evidence of hyperplasia in either the spleen or lymph glands. *This proves, it seems conclusively, that we have here a lymphocytosis arising from proliferation of lymphoid cells in the bone marrow, and death occurring before any other organ in the body showed involvement.*

We now wish to consider the nature of the changes in the bone marrow and the histogenesis of the cells proliferating in such instances.

The normal structure of the bone marrow is less well understood than any other tissue in the body. This ignorance is due partly to the complexity of structure, partly to the difficulties presented in attempting to make either smear preparations or sections of this tissue.

It seems strange that the school of Ehrlich which has so completely described the different cellular elements of the blood, has done so little in applying its staining methods to the bone marrow, which they themselves acknowledge to be the origin of most of the blood elements. Lazarus[1] dismisses the subject of the bone marrow changes in myelogenous leukæmia, with the statement that the pathological changes here are similar to those that occur in the blood. Ehrlich bases his claim

[1] Spec. Pathol. u. Ther. von Nothnagel, 1901, Bd. viii. p. 111.

that lymphatic leukæmia arises in the lymph glands by asserting that no lymphocytes occur normally in the bone marrow, and that, therefore, the process here is one of invasion or metastatic growth of lymphadenoid tissue.

In the papers of Arnold,[1] Engel,[2] Pappenheim,[3] Nägeli,[4] Rubinstein,[5] and others, which deal with the structure of the bone marrow, we find unanimous agreement as to the normal occurrence in this tissue of lymphoid cells, practically identical morphologically with the lymphocytes. These cells are always present and in considerable number. The authors differ as to whether they are in reality lymphocytes. Nägeli prefers to call them myeloblasts, but his objections are trivial and cannot be sustained. Rubinstein also considers the bone-marrow cell different from the similar cell occurring in the blood and lymph gland, basing his statement on staining properties, which in our experience are not specific.

The whole question which has been of grave importance to histologists for years as to the dual origin of the blood leucocytes—granular cells coming from the bone marrow, and non-granular cells, lymphocytes, coming from the lymphatic tissue—pivots on this point. The summary of evidence seems to be as follows:

Contrary to the view of Ehrlich, bone marrow contains lymphoid elements, identical morphologically with the lymphocyte. Indeed, some authors emphasize the lymphadenoid nature of bone marrow, strengthening their claim by asserting that in certain diseases, such as lymphatic leukæmia, bone marrow reverts to the fœtal type and becomes lymphoid tissue, the mother cells or lymphoid cells losing their power to differentiate into granular cells. These lymphoid elements are believed by the best authorities on bone marrow to be the mother cell of all granular elements of the bone marrow, and through them of the transitional and granular cells of the blood. The question of the identity of the lymphocyte of the blood and the lymphoid cells of the bone marrow is not to be established as long as we are using two different standards in considering this point. Morphologically, they are identical. If, however, as Michälis and Wolff[6] suggest, the future of the cell is the criterion—that is, if we define a lymphocyte as a cell which cannot develop into a granular cell—the lymphoid cell of the bone marrow and of the lymph glands are presumably distinct. The lymphocyte of the blood which we know never develops into the older granular cells, is, perhaps, the only cell which deserves this restricted title.

[1] Virchow's Archiv, 1895, Bd. cxl. p. 411.
[2] Deutsche med. Wochenschr., 1898, No. 47, p. 745.
[3] Virchow's Archiv, 1899, Bd. clvii. p. 19; 1900, Bd. clix. p. 40; 1901, Bd. clxvi p. 424.
[4] Deutsche med. Wochenschr., 1900, No. 18, p. 287.
[5] Zeitschrift f. klin. Med., 1901, Bd. xlii. p. 161.
[6] Deutsche med. Wochenschr., 1901, No. 38, p. 651.

The question then is, does this true lymphocyte of the blood come from the lymph gland only, or from all the hæmopoetic organs. The weight of opinion derives it essentially from the lymph follicle. However, there is very little to establish this view, and the facts brought forward either allow of another explanation or need further confirmation. The gland origin of lymphocytes is based by Ehrlich[1] on the grounds that whenever we have increased function of lymphatic tissue, such as in active digestion, whooping-cough, hyperplasia of glands, etc., we have a resulting lymphocytosis, and also that destruction of lymphatic tissue as in malignant disease, or in the intestinal diseases of children causes a lymphæmia. The action of tuberculin and pilocarpin in increasing the lymphocytes in the blood he traces in an obscure way also to the hyperplasia of the lymphoid tissue. He asserts that an increase in the lymphocytes in the blood is always a passive leucocytosis, due to an over-production of these elements, and a mechanical overflow of them into the blood. The interesting observation of Hirschfeld[2] on the amœboid action of lymphocytes in a case of lymphatic leukæmia is of importance in the question of the essential difference between active and passive leucocytosis.

Of late considerable doubt has been thrown on these alleged facts substantiating the origin of lymphocytes from the glands. Knox and Warfield[3] have shown that in intestinal diseases of children a true leucocytosis usually occurs. The existence of a constant digestion leucocytosis is rendered doubtful, and when present may not consist in an increase in lymphocytes.[4] The lymphæmia in malignant diseases if present may have several explanations. In sarcoma of the lymph glands and in Hodgkin's disease, where there is enormous hyperplasia of the lymphoid cells, the lymphocytes are practically never absolutely increased, and even a relative increase, as claimed by Pinkus[5] as invariable in Hodgkin's disease, is not constant. Moreover, it is difficult to understand the mechanism regulating the overflow of the lymphocytes either temporarily or permanently from the gland into the blood. The anatomical structure does not permit these elements, if they are non-amœboid, to pass into the circulation from the lymph gland except through the medium of the thoracic duct; while in the bone marrow, where the lymphoid cells are normally present, the parenchyma and bloodvessels are in more or less free communication.

We cannot state positively that the lymphocyte of the blood comes from the bone marrow, but we would urge to the attention of the medical world

[1] Spec. Path. u. Ther. von Nothnagel, 1901, vol. viii. p. 67.
[2] Berl. klin. Wochenschr., 1901, No. 40, p. 1019.
[3] Johns Hopkins Hospital Bulletin. In press.
[4] Japha. Jahrbuch f. Kinderheilkunde, 1900, Bd. lii. p. 242.
[5] Spec. Pathol. u. Ther. von Nothnagel, 1901, Bd. viii. p. 3.

that we have no proof that the lymphocyte comes from the lymph gland alone, and that all the other colorless cells of the adult blood originate in the bone marrow from lymphoid cells.

Our knowledge of the structure of bone marrow is greatly increased by the study of certain diseased conditions where we find various reversions to a fœtal type of tissue, which if correctly interpreted must help elucidate the histogenesis of the normal structure. In inflammations and new-growths little is to be learned along these lines. In Rubinstein's[1] interesting work on experimental leucocytosis, and in the numerous studies in the changes in anæmia, we find an interesting picture of functional hyperplasia. In one case the blood-forming organ is attempting to make up for the continuous drain of leucocytes, and in the other case of erythrocytes. In both instances, the lymphoid elements of the bone marrow show considerable increase.

Rubinstein emphasizes the possibility of a forerunner of both the white and red cells in a colorless mother cell. This identity of the leucoblast and erythroblast (Löwit) is not a new idea, but one which is as yet undetermined. Pappenheim believes that in embryonic bone marrow direct changes from basophilic lymphocytes to nucleated red cells may be observed. *In our case, the similarity in form of the small lymphoid cells with the normoblasts, which were conspicuously few in number, was suggestive. It is not impossible that the increase here was in a mother cell, from which the lymphoid cell and the hæmoglobin-containing cell are normally derived.* In normal bone marrow we are always able to find a few cells apparently identical with the small lymphoid cell described in this case, and differing sharply from the other lymphoid cells present. In different diseased conditions of the bone marrow, with the exception of grave anæmia, there was no increase in the number of these cells. In several cases of pernicious anæmia examined, such cells seemed to be present in greater number, but it was extremely difficult to tell them from the young normoblasts, which were also abundant. The color of the protoplasm of a hæmoglobin-containing cell, especially in stained sections, is a slight and variable criterion on which to base such a distinction.

In leukæmia we undoubtedly have in the bone marrow a hyperplasia, differing from that in leucocytosis and anæmia qualitatively. In the cases in which myelocytes are the predominating feature of the blood, the elements of the bone marrow are all increased, but the myelocyte is the prevailing cell type. Our own observation confirms the descriptions in the literature on this subject. In leukæmia where the lymphocytes of the blood are increased, there is always a corresponding increase in the lymphoid cells of the bone marrow, the other elements

[1] Loc. cit.

being relatively diminished. In both forms of leukæmia, then, we find an increase in the parenchyma cells of the bone marrow, but a proliferation differing qualitatively in the type of cell especially increased. In one case we have a reversion of yellow marrow to red, with an increase in the older elements of the organ; in the other we have a reversion of all the marrow to a lymphadenoid condition—presumably a fœtal stage—in which the young, undifferentiated elements are predominant.

To explain these changes, if we assume the process to be similar in both cases, we find in Rubinstein's work suggestive lines of thought. Acute leukæmia always resembles strongly an acute infectious disease; indeed, all forms of leukæmia admit of some such explanation. Rubinstein proved by injecting a substance chemotactically positive for polymorphonuclear leucocytes, that these were drawn forth from their reservoir in the bone marrow, and that by continually draining this supply, a proliferation of the elements from which these cells arose would occur. It is possible that in leukæmia there may be a similar chemotaxis from some diseased condition in the body, which calls forth certain elements from the bone marrow, and also accounts for the proliferation of these elements to make up the deficiency which their constant drain must otherwise cause in the bone marrow cells.

That hyperplasia of the bone marrow alone even with qualitative changes in the relation of the different cellular elements is not sufficient to account for the change in the blood picture, is shown by the microscopic examination in lymphosarcoma, myeloma, etc. In such conditions, if the increase of the blood cells depended only on mechanical over-production in the blood-forming cells, there would be no explanation for the fact that the blood, as a rule, shows no particular change. Some such influence as chemotaxis must be admitted to explain a leucocytosis, whether it consists of polymorphonuclear elements, or of more unusual forms.

We must now consider the unity of the two forms of leukæmia which hitherto we have assumed. Myelocytic leukæmia is now granted by all to be of primary bone marrow origin. The case reported by Hirschfeld[1] of acute myelogenous leukæmia, confirming two similar cases cited by Cabot,[2] furnishes the evidence which has long been awaited, that myelocytic leukæmia may also appear as a fulminating disease.

In the so-called lymphatic leukæmia, there is almost unanimity of opinion that the blood is not leukæmic until the bone marrow is involved. Cases such as the one here reported, where the bone marrow was extensively involved without enlargement of the lymph glands, have

[1] Berl. klin. Wochenshr., 1902, No. 11, p. 231.
[2] Boston Med. and Surg. Journal, 1894, vol. cxxxi. p. 507.

been recorded by Goldschmidt,[1] Körmözi,[2] Walz,[3] Pappenheim,[4] Hirchlaff,[5] and Spencer.[6] Quite a number of cases are to be found in the literature where the glands have been slightly enlarged, or at least the increase has been inadequate in relation to the marked blood changes. *We believe such cases go to prove that acute leukæmia, whether lymphoid or myelocytic, is due to changes in the bone marrow, the other hæmopoetic organs being involved, if at all, secondarily.* In chronic lymphatic leukæmia the evidence is less satisfactory. Here we may revert to Neumann's statement that no case in which the bone marrow was not involved is on record, and argue from analogy that, as in the acute form, the bone marrow is presumably the primary seat of the disease to which the clinical features are due.

The possibility of a pseudoleukæmic form of chronic lymphatic leukæmia is always being urged. The word pseudoleukæmia is a very loose term and must be strictly defined before being used. We[7] believe that Hodgkin's disease is a specific disease, with characteristic pathological changes, easily recognized, and never having the blood picture of leukæmia. It is as impossible to think of this form of pseudoleukæmia changing to leukæmia as to think of tuberculosis or sarcoma of the glands undergoing such a transformation. Leukæmia, of course, may be superimposed on any other specific enlargement of the glands, but such cases, if occurring, have no bearing on the question in point. Pseudoleukæmia, then, in the sense of a simple hyperplasia of the glands, preceding the bone marrow changes which result in leukæmic blood, has yet to be established. We cannot deny the possibility, although such a condition would be inconsistent with our conception of the nature of the disease, and if proven to occur would necessitate another explanation of the facts which now fit into our present view of the subject.

On the other hand, cases described by Michälis,[8] Hirschfeld,[9] and others, in which the blood shows a divergence from either of the well-established forms of leukæmia in presenting a mixed-cell leucocytosis, strengthens our belief that all leukæmias are due to the action of some unknown poison on the bone marrow. The myelogenous changes result in the blood differences by which the disease is recognized. The involvement of the other organs by hyperplasia or infiltration is secondary, and not essential to the disease.

We have no right, then, to apply the term myelogenous to one form of the disease. *We would suggest that there are three forms of leu-*

[1] Münch. med. Wochenschr., 1896, Bd. xliii. p. 714.
[2] Deutsche med. Wochenschr., 1899, No. 15, p. 238.
[3] Loc. cit.
[4] Loc. cit.
[5] Centralbl. f. inn. Med., 1898, Bd. xix. p. 856.
[6] Lancet, 1900, p. 926.
[7] Johns Hopkins Reports, 1902, vol. x. p. 133.
[8] Zeitschrift f. klin. Med., 1902, Bd. xlv. p. 86.
[9] Loc. cit.

kæmia, all due to myelogenous changes, and that these should be known as the myelocytic, lymphoid, and mixed-cell varieties, if we wish to make the blood picture the basis for clinical divisions. Any of these three forms may be either acute or chronic; the myelocytic is usually chronic, the lymphoid usually acute. The nature of the disease, the etiology, and the primary focus in the body we believe to be still undiscovered. Leukæmia as we know it is simply the manifestation of some poison which affects especially the bone marrow, the blood-forming organ in the adult, and ultimately causes death.

REPORT OF A CASE OF SEVERE, PROBABLY PERNICIOUS ANÆMIA, WITH MARKED GENERAL AND CORONARY ATHEROMA, IN WHICH MANY EVIDENCES OF ANEURISM WERE PRESENT WITHOUT ANATOMICAL EXPLANATION FOR THEM.

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Jessie W., a Canadian laborer, aged thirty-one years, married, entered Ward 6 in my Cook County Hospital service March 3, 1897. His previous history was somewhat meagre. Eight years previously he had a single venereal sore two or three months, after which he had rheumatism, and somewhat later an attack of pleurisy, the location of which he could not recall. An alcoholic and tobacco history was elicited.

As to his present history, he had grown weaker, but had not lost any great amount of flesh. Some pain had existed for weeks or months over the lower left chest. The appetite had declined, but anorexia was not absolute, nor did it concern any special variety of food. He vomited once, and eructations of gas were frequent. There had been some slight dyspnœa, increased by exertion and the erect posture. The skin for a week had been somewhat yellow, and the urine was dark, but the bowel movements were not noted. Direct questioning developed no other points.

Physical Examination. The patient lay in a somewhat listless state. His breathing was moderately accelerated, ranging between 25 and 32 respirations a minute. The skin and mucosæ were distinctly yet not deeply icteric. The tongue was covered with a yellowish-white fur. The hair was somewhat thin. Examination in other respects was negative regarding the head, scalp, ears, eyes, and throat. The lungs were wholly negative, except that respiratory excursion was absent over the left lower lobe, laterally and posteriorly. The peripheral arteries pulsated actively, yet arterial tension was low. The initial pulse-rate ran between 90 and 112. The radials and brachials alone were tortuous

and rigid to the finger. No inequality in tension nor in the size of the pulse-wave was noticed in any of the arteries, including the femorals.

The heart was normal in its outlines, save that the left border and apex-beat were found in the left nipple line. A soft blowing systolic murmur was heard with equal distinctness over the pulmonic and mitral areas, and the second aortic tone was loud and almost metallic.

Over the left lower chest was observed a diffuse and most distinct pulsation which, as the patient lay on his right side, extended horizontally from the lower angle of the left scapula around the chest into Traube's space and the epigastrium and in a downward direction to a point distinctly below the left costal arch. The pulsation was vigorous and distinctly expansile to both the eye and hand. A systolic bruit was heard over the pulsating area, but was most clearly audible over the left chest behind. No thrill was detected at any time.

The liver's edge was barely palpable on deep inspiration, was even and of normal resistance. The spleen could not be felt. Otherwise, the abdomen was negative. The urine was 1020 c.c.; specific gravity, 1016; a trace of albumin; urea, 1.07 per cent. No sugar, no peptone, etc.; a moderate number of small granular casts was found.

The nervous system was negative.

The stools were not acholic.

The patient was demonstrated in my clinic as aneurism either high in the abdominal aorta or possibly low in the thoracic aorta. Dr. Robert B. Preble, of the attending staff, also examined the case and demonstrated it as aneurism. When in clinic the pulsation could be clearly seen twenty or thirty feet and its striking expansile throb was demonstrated by pasting on the anterior and posterior surface of the lower chest small pieces of bent paper which were widely separated with each cardiac systole. This experiment was performed to demonstrate the expansion to the eye rather than to the hand of the student. The blood was not examined at first but a few days before the patient's death, his temperature, which had occasionally reached 100° and 100.6° F., fell to 97° F. by mouth, his pulse became thready and could scarcely be counted. The respirations became rapid and shallow, with all of the classical symptoms of collapse. Upon reaction the pulsation was less distinct and a decided anæmic appearance was then first noted, possibly having been obscured by the previously icteric hue, which had now largely disappeared. Examination of the femoral and other vessels was carefully made, with the thought that retroperitoneal or other rupture had occurred. The femorals were equal and synchronous with each other and the radials, etc. The blood showed 5000 leucocytes to the cubic millimetre, a differential count of which revealed normal relations. The red cells numbered 1,400,000, and the hæmoglobin by Fleischl's instrument registered 32 per cent. In the stained preparation the red cells varied but little in size and dimension. There was not much poikilocytosis. A large number of nucleated red corpuscles was seen, the great bulk of which were normoblasts, few megaloblasts being detected.

The patient collapsed again and died rather suddenly, March 21st, eighteen days after admission.

The clinical diagnosis was formulated as follows: 1. Arteriosclerosis. 2. Abdominal aneurism, probably pointing toward the diaphragm. Little stress was placed upon the mere fact of the pulsa-

tion, but the perfectly clear expansion of the pulsation seemed to establish the diagnosis of aneurism beyond doubt, with rupture explaining the collapse. 3. Dilatation of the left ventricle. 4. Catarrhal icterus. 5. Acute secondary anæmia. The possibility of pernicious anæmia was discussed and considerable uncertainty was experienced, still it seemed to all who examined the case that the evidences of aneurism, followed by collapse from rupture and sudden death, outweighed all other considerations.

Post-mortem. No. 104, March 22d, one day after death, attended by Drs. Preble, Brown, Hammond, Hunter, Champlin, Smith, Humiston, McGrady, Kirby, and the writer.

Some emaciation ; well-marked rigor mortis. The pericardium contained 4 grammes of clear serum. The heart weighed 600 grammes; the endocardium presented the tabby-cat appearance; the myocardium was very pale. Very small yellow plaques were found at the base of the mitral valves and in the beginning of the aorta.

In the left coronary artery, one inch below its origin, was a long plaque or series of plaques of yellow color, hard, some elevated and the size of a pin-head, while others were diffuse and larger. Similar changes were found in the right coronary one and one-half inches below its origin. Over the entire length of the abdominal and thoracic aorta were scattered small yellow areas, some of which were hard, rough, elevated, and breaking with a distinct sound and almost nodular.

Nowhere were any bulgings nor aneurism of the aorta. Similar changes existed in the common iliacs, external and internal iliacs, the femoral arteries and a few of the larger branches of the latter. The nose, larynx, and trachea were negative. The bronchial glands were slightly enlarged and on section anthracotic. The mediastinum was negative. The right pleural cavity contained 300 c.c. of clear serum and no adhesions existed. A few old, thin adhesions were found over the left apex, and the base of the left lung was adherent by well-organized tissue to the chest wall and the diaphragm. The adhesions were œdematous. Above these basal adhesions was a small amount of clear serum. The right lung weighed 530 grammes, the left lung 660 grammes. The lungs floated, crepitated throughout, and on section appeared light gray, a frothy yellow serum being readily expressed, particularly from the left lower lobe. The tongue and the pharynx were negative.

The œsophagus and stomach were exceedingly pale, as was the mucosa of the small and large gut, save for some hypostatic post-mortem discoloration. Small, hard plaques similar to those found in the aorta were seen in the superior mesentery artery and its larger branches. The peritoneum was smooth, and the abdominal cavity contained no fluid. The bile-ducts were patent, and the gall-bladder slightly distended with somewhat viscid bile. The liver weighed 1940 grammes, and its surface was light red and mottled. No adhesions were found, and the liver's edge was smooth and sharp. Its consistence was firm, and on section contained but a moderate amount of blood. On section the lobular markings were fairly distinct, the centre showing red and the periphery light. The pancreas was negative, weighing 120 grammes. The spleen weighed 180 grammes, and there were some perisplenitic adhesions, but to the diaphragm only. The organ was dark purple in color, and the parenchyma soft and friable. The left kidney weighed

200 grammes, the right 160 grammes. The capsule was easily stripped, leaving a smooth, very pale, and slightly mottled surface. The section was very pale, the cortical markings were obliterated, and the cortex and medullary portion were as 1 to 3. The pelvis, ureters, bladder, prostate, seminal vesicles, and urethra were negative.

The brain weighed 1650 grammes, and its examination was wholly negative, especial attention having been directed to the bloodvessels. The spine and cord could not be examined.

The long bones could not be examined, but the section of the sternum showed the reddish jelly-like marrow seen in pernicious and other severe anæmias.

The anatomical diagnosis read: Atheroma of the coronary arteries, mitral valves, aorta and its main lower branches; left ventricle hypertrophy and dilatation; fatty degeneration of the myocardium; pulmonary œdema; partial left adhesive pleuritis; chronic nephritis; acute splenic tumor; perisplenitis; marked anæmia of the alimentary tract, etc., pernicious anæmia (?).

The case presents no remarkable pathological features. The vascular changes were very marked for a person aged thirty-one years, and may be referred with some degree of correctness to syphilis. While the blood findings were not exactly characteristic of pernicious anæmia, still they corresponded fairly well with the subacute or milder recurrent type of pernicious anæmia as described by Cabot and others. The exact cause of the collapse, considered by us as due to aneurismal rupture, which led to sudden death in its second occurrence, may have been due to extensive bilateral coronary disease or to this cause combined with the profound anæmia.

The chief clinical interest of the case centres in the pulsation. The pulsation was extensive, attended by a bruit, abdominal as well as thoracic, and markedly expansile.

At first thought it might seem that the pulsation resembled Broadbent's sign, but the pleural adhesion was purely basal, and there was neither pericardial synechia nor indurative mediastinitis. When a pulsable movement, says Broadbent, is seen in the lower posterior chest it may appear at first sight to be expansile, but on more careful scrutiny it is found that there is a tug upon the false ribs during the systole and a sharp rebound during the diastole, etc.

It has been impossible for me to look over the literature bearing upon this unique case, for a lack of a title covering its phenomena. Personal inquiry of a number of experienced clinicians, as Professor Osler, has not developed any similar instance.

The pleural adhesions and lack of respiratory excursion at the base of the left lung was noted clinically, but did not excite any remark, since among the lung changes incident to aneurism, pleurisy with effusion, adhesive pleurisy, lung induration, etc., have been repeatedly described by writers on aneurism since the classical work by

Stokes. The adhesions were thought to be either due (1) to aneurism near the diaphragm, or (2) to mere coincidence. Nothing suggested pulsating neoplasm of the lung or pleura. A pulsating pneumonia as described by Graves was merely mentioned in the clinic as one of the causes of thoracic pulsation, as were pulsations of the liver and spleen in Basedow's disease, aortic and tricuspid regurgitation as rare causes for abdominal pulsation. Mention was then made of the empyeme pulsatile (Aran), the pulsating empyema of Stokes, and the empyema necessitatis pulsans of MacDonnell.

Dr. J. C. Wilson has reviewed with great care the subject of pulsating pleural effusions.

The literature of pleuritis pulsans brings out the fact that most instances (about 92 per cent.) are left-sided. A review of the causes suggested concerns:

1. The theory of Traube, which referred the pulsation to the condition of the heart and pericardium.

2. Comby's theory placed stress upon adhesions to the pericardium and compression of the lung.

3. Féréol's explanation was pneumothorax with a large effusion, these conditions being imperative.

4. Wilson's conditions: (*a*) Some paresis of the intercostal muscles, as results from a long-standing pleuritis; (*b*) local necrosis and perforation of the parietal pleura (empyema necessitatis); (*c*) pneumothorax; (*d*) atelectasis of the lung, which is in relation with and adherent to the pericardium.

Aneurism has often been thought of, but the statement constantly recurs that it can usually be excluded, except when an encysted empyema lies close to the heart. Among the conditions just named practically the only one in our case was the pleural adhesions over the base of the left lung. I have been able to reach no satisfactory explanation of this pulsation, although the active arterial pulsation might have been propagated by means of the adhesions to the chest and by means of the perisplenitic connective tissue to the abdomen. This suspicion, however, in no way accounts for the *expansile character of the pulsation*, which of yore has been held to invariably (ref. 14 and 15) exclude dynamic pulsation.

In the discussion, Dr. Lafleur, of Montreal, recounted a case in which the pulsation was exactly similar to our case, and other signs, as hæmatemesis, paralysis of the left vocal cord, etc., were present. The pulsation was expansile, but the diagnosis of aneurism was incorrect, the autopsy showing gastric ulcer.

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THE PATHOLOGY OF PERNICIOUS ANÆMIA, WITH SPECIAL REFERENCE TO CHANGES OCCURRING IN THE HÆMO-LYMPH NODES (EIGHT AUTOPSY CASES).[1]

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THE pathology of pernicious anæmia as given in the most commonly used text-books of to-day contains but scant reference to the lymph glands and no mention at all of the hæmolymph nodes. Though much attention has been paid in recent years to the changes occurring in the spleen and bone marrow, the lymphatic structures have been practically disregarded as a possible factor in the pathogenesis of this disease.

In Barclay's case of "Death from Anæmia" (1851) no mention is made of changes in the lymph glands.

The classical description by Addison (1855) states that in "idiopathic anæmia" there is no "renal, splenic, miasmatic, glandular, strumous, or malignant disease."

In one of Wilks' cases (1857) the lymph glands were described as "healthy." Lebert (1858) does not mention the lymph glands. Bristowe, in the same year, reported a case in which the bronchial, mesenteric, and other abdominal glands were described as "healthy." No mention of lymph-gland changes is made by Cazenave in 1860. In the same year Habershon states that there is no lymphatic disease in "idiopathic anæmia." Grohe (1861) does not mention the lymphatic glands

[1] Read by title at the meeting of the Association of American Physicians, Washington, D. C., April 29, 1902.

in the report of his case. Neither is there any mention of lymphatic-gland changes in the cases observed by Wagner (1864), Trousseau (1868), and Perroud (1869).

Biermer's celebrated observations on "Progressive Pernicious Anæmia" (1868–1872) contain no mention of the condition of the lymph glands. Likewise in the cases reported by King and Gusserow (1871) no mention is made of these structures. In an unpublished case of Pye-Smith, observed in the same year, slight enlargement of the lumbar glands was noted. In Sörensen's case (1874) no swelling of the lymph glands was noticed. Immermann, in the same year, does not mention the condition of the lymph glands.

In 1875 Pepper stated positively that in pernicious anæmia there is "no affection whatever of the lymphatic glands." Immermann, in Ziemssen's *Cyclopædia*, stated that "the spleen, the lymphatic glands, the marrow of the bones, show no signs of hyperplastic activity or of anything abnormal beyond extreme paleness." In the same year Krieg mentions the mesenteric glands in one case as atrophic; and Schumann found in one case that the "mesenteric glands were enlarged, grayish-white, spotted with red, and hemorrhagic." Two cases reported by Pye-Smith showed no change in the lymphatic nodes.

In 1876 cases were reported by Lebert, Burger, Scheby-Buch, and Bradbury without mention of the lymphatic glands. In the same year Ferrand reported a case with "swelling of the mesenteric glands," and Habershon one in which "no glandular enlargement was found." Quincke (1877) observed one case with "slight swelling of the lymph glands." Cases were reported in this year by Mackern, Stricker, Rosenstein, and Andrew without mention of the lymph glands; Bramwell, one case in which the mesenteric glands were somewhat enlarged, and Purser a case in which the bronchial glands were mentioned as normal and the mesenteric glands not enlarged.

Lépine's review of the fifty cases published up to this year contains the statement that under "essential anæmia" should be included also cases in which there was a decided affection of the spleen, lymph glands, or marrow. No details of these changes are given.

In 1877 appeared also the first monograph on pernicious anæmia—that of Müller. Sixty-two cases, with thirty-nine autopsies, were analyzed. In only one case was the condition of the lymph glands mentioned—Case XXXIV.—in which the mesenteric glands were of a striking bright-red color.

In 1878 the more elaborate work of Eichhorst—*Die Progressive Perniciöze Anämie*—was published. This work was based upon the analysis of eighty-four cases collected from the literature (including those of Müller) and seven cases of his own—eighty-nine autopsies in all. The changes occurring in the lymph glands were summed up by

Eichhorst as follows, and inasmuch as this summary forms the chief basis for the statements found in subsequent text-books, it is quoted in full:

"*Lymph Glands.* In the superficial lymph glands, which may be easily and thoroughly examined by the hand, no enlargement in pernicious anæmia has been found. In my fourth observation the glands of the groin were hard and scarcely larger than peas, yet any one who has examined many patients knows that this condition is a very common, almost normal occurrence.

"Even so rarely have I seen enlargement of the mediastinal and thoracic glands in my autopsy cases or have found such condition mentioned in the literature.

"From this the impression is gathered that the lymph glands in the above-mentioned regions are able to offer a greater resistance to the irritation caused by the changed quality of the blood than is the case with the spleen, although they correspond so closely in structure with the latter.

"Quite different is the case with the mesenteric glands. Repeatedly have changes been found in them in pernicious anæmia; and it is possible that the number of such observations would be greater if, as there is good reason to suspect, they had not frequently been left unexamined.

"Krieg found them atrophic in a man who had dilatation of the stomach.

"Müller observed in one case that they appeared very prominent because of the contrast of their bright color against the surrounding anæmic tissues.

"Ferrand and Quincke state that the glands were swollen. Schumann found likewise a swelling of the mesenteric lymph glands. On section they appeared of a grayish-white color, speckled and spotted with red. In the last three observations it is important to make prominent the fact that the swelling of the lymph glands existed independently of any splenic enlargement, the latter not being present in these cases. Moreover, disturbances of digestion were not present to any degree worthy of mention in the cases of Quincke and Schumann.

"Swelling of the mesenteric lymph glands was noticed in three of my five cases which came to autopsy. They reached the size of a hazelnut. The glands were of rather firm consistency, and on section appeared bright red. It seemed remarkable to me that the red color was not homogeneous, but spotted, without it being possible either with the naked eye or with the help of the microscope to discover true hemorrhages. No unusual cellular elements were found in the glands, and their enlargement depended upon a hyperplastic condition.

"With relation to the causes of this hyperplasia I might here assume the explanation which I have offered for the origin of the splenic hyperplasia. I take it that we have here to do with subsequent conditions and secondary changes dependent upon the abnormal constitution of the blood.

"In my fifth observation the simple hyperplasia was accompanied by another anatomical appearance: small caseous areas were found in the swollen glands. I have been able to collect from the literature many cases, from which it appears that even hyperplastic lymph glands

are inclined to other metamorphoses. Slawjansky, many years ago, described two cases of leukæmia lienolymphatica, in which the enlarged lymph glands showed in many places a pronounced caseous metamorphosis. Schnitzer has reported from Frerich's clinic a case of pseudoleukæmia in which the enlarged lymph glands in the neighborhood of the cardia appeared medullary infiltrated. Caton has under the same conditions observed amyloid change in the lymph-gland tumors."

In 1878 three cases were reported by Mackenzie, who summarized the clinical and pathological features of the disease, stating "that the lymphatic glands are usually not enlarged."

In 1880 Weigert reported a remarkable case, which is noteworthy as being the first case of pernicious anæmia in which changes of importance were noted in the lymph glands. As this case is constantly referred to in the subsequent literature, I quote in full those portions of his description relating to the lymphatic changes:

"The axillary and inguinal glands are swollen to red masses, and are surrounded by a delicate network of dilated lymph vessels filled with red, transparent fluid. . . . Cervical lymph glands swollen to red masses, surrounded, especially from above, by a very delicate network of greatly dilated lymph vessels filled with red, transparent fluid. On the right side of the ascending aorta, in the upper half of the thoracic portion of the same, lies a very rich, remarkable network of knobby lymph vessels filled with a clear, red fluid, these communicating frequently with the thoracic duct. The network has a breadth of 2 cm. . . . Mesenteric, retroperitoneal, portal, and omental lymph glands and vessels similar to the above. . . . The microscopical examination of the lymph glands showed a marked dilatation of the lymph sinus and the presence in the same of a lymph uncommonly rich in blood. A similar fluid was observed in the lymph vessels."

In explanation of this case Weigert ruled out the hemorrhages present as the causal factor, in that they were too small to account for the presence of so much blood in the lymphatics, and in many places no hemorrhages were present in the area supplying the lymphatics, though the latter were filled with blood. At first inclined to explain the process as due to an increased permeability of the vessel walls for red cells and blood plasma, but not to such a degree as to form visible hemorrhages, Weigert was led later to regard it as due most probably to a compensatory hæmatopoetic function of the lymph glands for the marrow. He was not able to make out the presence of nucleated red cells. The dilatation of the lymph vessels was, at any rate, not due to obstruction.

Hartshorne, in Reynolds' *System of Medicine* (1880), states that there is "no alteration of lymphatic glands" in pernicious anæmia Coupland, in the Goulstonian lectures on anæmia (1881), says that there are no changes in the lymphatic glands in this disease.

In 1883 Pye-Smith gave a clinical and pathological analysis of the

disease, based upon a study of 103 autopsy cases collected from the literature (including Müller's and Eichhorst's) and one new case observed by himself, concluding from this analysis that "in genuine cases of idiopathic anæmia the lymph glands are not enlarged, nor are the solitary or agminated lymph follicles. Slight swelling of the mesenteric lympharia has been occasionally noticed, due, perhaps, to precedent diarrhœa."

Osler, in Pepper's *System of Medicine* (1885), says: "The lymph glands are, as a rule, normal in size and appearance. In three instances I have found them decidedly smaller than normal, and in two they had a rich red color, and on section looked more like spleen tissue than lymph gland. Weigert has noticed the same appearance. In one of the cases there were nucleated red corpuscles in the glands, as has been observed by Rindfleisch in a case of rickets and more recently in tuberculosis."

In Fagge's *Practice* (1886) the lymph glands are not mentioned in the article on pernicious anæmia. In the same year Flint says: "The lymph glands, which are usually normal in appearance, may be somewhat swollen and of a deep red color, containing an unusual number of red blood corpuscles, among which may be nucleated red corpuscles." In 1887 Bartholow says that the "disease is distinguished from leukæmia by the normal condition of the spleen, liver, and lymphatics."

Eichhorst (1891): "Mesenteric glands often swollen, hyperæmic in places, and speckled with blood. In one case all the glands were swollen and red, the lymphatics dilated and contained bloody lymph."

Osler (Pepper's *American Text-book*, 1894): "The lymph glands may be unchanged, though in three of my cases they were of a deep red color, resembling spleen tissue—a condition which has been noted by Weigert."

Grawitz (1896) refers to Weigert's and Neumann's cases. Tyson, in the same year, says there is "absence of lymphatic enlargement or involvement of the spleen except in a small degree."

Anders' *Practice* (1897): "The lymph glands are often somewhat swollen and intensely red in color, owing to the unusual number of red corpuscles, some of which are nucleated."

Ehrlich and Lazarus (Nothnagel's *Specielle Pathologie und Therapie*, (1898): "In a fairly large number of cases which otherwise showed nothing characteristic, especially no splenic enlargement, the mesenteric lymph glands were found to be swollen (Eichhorst, Quincke, etc.). From the microscopic examination of the first-named observer the enlargement appeared as a pure hyperplasia; only in one case were the swollen glands caseous in the centre. What relation these enlargements of the lymph glands bear to the disease process, or whether they stand related to local disturbances in the intestinal tract, or to the dis-

turbed abnormal function of the bone marrow, cannot be decided. The blood findings give no evidence of increased activity of the lymph glands in so far as the production of lymphocytes is concerned."

Eichhorst (Eulenberg's *Real Encyclopædia*, 1898): "Swelling of the mesenteric glands repeatedly found. Other lymph glands also sometimes enlarged. Weigert describes the presence of bloody lymph in the dilated lymph vessels."

Strümpell: "The lymph glands do not usually present any changes in pernicious anæmia. If they are much altered it is probable that the disease is quite a different one (pseudoleukæmia)."

In Bramwell's *Anæmia and Diseases of the Blood-forming Organs* (1899) no mention is made of changes in the lymph glands. Laache (Ebstein and Schwalbe's *Handbook*, 1900) states that the mesenteric glands are often swollen, and refers to Weigert's case.

Howard (*Reference Handbook of the Medical Sciences*, 1900): "The lymph glands are usually normal. In a few instances the lymphatic glands of the mesentery have been recorded as enlarged, this change being due, as Pye-Smith suggests, to a previous diarrhœa. In one case the lumbar lymphatic glands were enlarged."

Osler (1901): "The lymph glands may be of a deep-red color."

Cabot (*American Text-book of Pathology*, 1901): "The spleen and lymph glands show no changes in the majority of cases."

Hunter (*Pernicious Anæmia*, 1901): "Few or no changes have been described in connection with the lymphatic glands. The absence of any enlargement or other marked change is a notable feature (Addison), distinguishing this form of anæmia at once from leucocythæmia and other forms of glandular anæmia, and this observation has been confirmed by all subsequent observers.

"In some cases, however (Eichhorst's), the mesenteric glands have presented some appearances of redness and swelling. Another case is described by Weigert in which, along with dilatation of the lymphatics of the neck and of the mesenteric, portal, omental, and retroperitoneal lymphatics, there was also some swelling of the mesenteric glands, their sinuses being filled with lymph containing many red corpuscles. This case Weigert was inclined to regard as one of supplementary blood formation on the part of the glands; but it stands alone, and no great value, therefore, can be attached to it. No abnormal microscopic appearances have been noted, and as regards the importance to be attached to the appearance of redness and swelling, it is only necessary to state that precisely similar changes were found by Neumann in the case of anæmia resulting from severe metrorrhagia, already referred to. In this case likewise, with the exception of a very few nucleated red corpuscles, no changes were found microscopically."

In many of the text-books published within the last several years

(Schmaus, Kaufmann, Ziegler, Musser, Stengel, Coplin, Thompson, Ewing, Coles, *Twentieth Century Practice*, etc.) no mention is made of changes in the lymph glands in this disease.

Reviewing critically those statements above in which changes are said to have occurred in the lymph glands, it will be seen that practically, with the exception of Osler's observations, our knowledge of lymph-gland changes in pernicious anæmia is based upon Eichhorst's summary and the case reported by Weigert. The statements regarding the frequent occurrence of swelling of the mesenteric glands, when sifted down in the autopsy reports in the literature, are in reality based upon but few observations of this condition; and Eichhorst's statement that these changes have been repeatedly observed is not borne out by the autopsy notes of the cases upon which he bases his summary. I have analyzed, with respect to this point, 173 autopsy cases of pernicious anæmia collected from the literature since the appearance of Eichhorst's monograph. In 142 of these cases no mention of the lymph glands is made. In 14 cases the statement is "no enlarged lymphatics" in 4, "mesenteric glands not enlarged" in 4, "lymph glands normal" in 4, "mesenteric and lumbar glands all healthy" in 1, "of normal size and consistency" in 1 (cases reported by White, Axtell, Roosevelt, Musser, Smith, Fischel, Gottlieb, Sasaki). The positive findings are as follows:

In two cases reported by Kahler (1880) the mesenteric glands were somewhat enlarged, appearing as red bodies in the mesenteric fat; in another case they were described as red. Smith (1880) reported enlargement of the bronchial glands; in one case reported by Starr the mesenteric glands appeared smaller than usual. In the thirty-eighth case reported by Hobson "large lymphatics in the posterior mediastinum, pressing on the right vagus, thoracic duct, and splanchnics; glands in the neck and axilla much enlarged." In the forty-fifth case the mesenteric glands were very large, and Peyer's patches were marked.

Müller (1889): In one case of bothriocephalus anæmia the retroperitoneal glands showed some medullary swelling, and the jugular lymph glands were very rich in blood, resembling the spleen. In two cases with syphilitic history the lymph glands, especially the jugular, showed inflammation, reddening, and hyperplasia of the follicles. In a case of Holt's (1891) the "mesenteric glands were enlarged, not cheesy. The liver showed collections of spheroidal cells, presumably the hyperplastic lymph nodes of Arnold."

White (1890) reports one case with enlargement of the mesenteric glands and Peyer's patches; Klein, one case in which the right cervical and inguinal, and especially the left cervical, were enlarged, gray-red, or grayish-yellow. In the left axilla two glands the size of beans were present.

In a case of Hills (1898) caseating tubercles were found in the axillary and mediastinal glands. No enlarged glands in the abdominal or inguinal regions. Nammack (1900), a case in which the "axillary lymph nodes were enlarged; peribronchial lymph nodes enlarged and anthracotic." In a case reported by Henry in the same year tuberculosis of the mesenteric and retroperitoneal glands without tuberculosis elsewhere was observed. Grawitz (1901) reported one case in which the mesenteric glands were greatly swollen.

Eliminating accidental or coincident processes, such as tuberculosis, lymphadenitis, etc., the number of reported cases in which the lymph glands showed changes that might be regarded as belonging to the pathology of pernicious anæmia becomes very small, indeed. This paucity of observations may be explained by the assumption that lymph gland changes are of very rare occurrence in this disease, or that the changes are of such a nature as to easily escape observation at autopsy, or that in many cases no adequate examination of the lymph glands has been made. It is very probable that both of the last assumptions constitute the true explanation; in the absence of any marked changes it is very likely that in many, if not the majority of autopsy cases of pernicious anæmia in which no mention is made of the lymph glands, these were either superficially examined or entirely overlooked. I am led to this conclusion by my own experience. In every one of eight autopsy cases of pernicious anæmia the prevertebral lymph glands, particularly the hæmolymph nodes (cervical, thoracic, or retroperitoneal), showed changes, either gross or microscopic, which might be regarded as belonging to the essential pathology of the disease. In only one of these cases, however, were the gross changes so marked as to be noticeable without special examination of the retroperitoneal glands. Such special dissection is usually not a part of the ordinary autopsy technique. In my cases particular attention was paid to the lymph glands of all the regions for the purpose of collecting statistics of the relative occurrence of hæmolymph glands in the human body.

The reports of the cases which follow were from Dr. Dock's clinic of internal medicine, in the University Hospital, and I am indebted to the records of this clinic for the case histories and blood examinations, which are given here in a greatly condensed form.

Case I.—Mr. O. N. R., aged fifty-four years, American parentage, salesman by occupation, was admitted to the medical clinic May 26, 1898. Family history good; previous history negative; had usual diseases of childhood and an attack of typhoid fever at the age of thirty-four years. No history of venereal disease.

During the last three years he has had gaseous eructations, heartburn, and persistent constipation. For the last three months has been troubled with piles. He has noticed blood at nearly every stool, but

has never lost any large amount at any one time. In December, 1897, he first noticed a gradually increasing paleness, and at the same time began to be troubled with dyspnœa, palpitation, and general weakness. These symptoms are gradually becoming more marked.

Physical Examination at Time of Admission. The patient is five feet eight inches tall; his weight is 132 pounds (one year ago he weighed 143 pounds). Very cachectic and emaciated. Mind clear. Muscles very small and soft; panniculus very thin; marked œdema of ankles. Skin is pale sallow, with yellowish tint. Nails very pale. Mucous membranes and tongue very pale; connective tissue under tongue yellowish. Scleræ yellowish. Examination of lungs is negative. There is no apex-beat; the heart dulness is not enlarged. Heart sounds impure; pulse 88, dicrotic, regular. Examination of abdomen negative. Rectal examination showed a number of deeply congested papillomatous masses, about three-quarters of an inch in diameter, on the rectal wall just above the internal sphincter.

Blood Examination. Red blood cells, 960,000; leucocytes, 5672; hæmoglobin, 20 per cent.; specific gravity, 1027. The red cells show a marked degree of poikilocytosis. Differential count: normoblasts, 3; megaloblasts, 5; polynuclear leucocytes, 70; large lymphocytes, 7; small lymphocytes, 32.

Urine. Small amount; clear, dark reddish. Chemical tests negative.

On June 2, 1898, the patient was operated upon for hemorrhoids. After the operation all traces of blood disappeared from the stools, and the patient became somewhat less yellow, but remained extremely pale. At the same time the number of megaloblasts became diminished. His general condition improved; there was less œdema. He was discharged on the 27th of June, with advice to continue treatment of iron, arsenic, and hydrochloric acid, and to return later.

He was readmitted on January 6, 1900. For four to five months after leaving the hospital, in June, 1898, he remained in bed, getting up at short intervals. During this time he gained in strength, but was troubled with profuse sweating and swelling of the legs. Gastro-intestinal symptoms were marked. In October, 1898, he went to Texas for three months. There he continued to gain in strength, but at no time was he able to be up long. Breathlessness and palpitation continued. After his return, up to the fall of 1899, he remained about the same. At this time he began to grow weaker, and the symptoms of shortness of breath, palpitation, etc., increased, with severe pain in the heart region on slight exertion. Has irregular elevations of temperature. During the last six months he has noticed a gradual pigmentation of his body, first on his arms and over the inner surfaces of the thighs, and gradually appearing over the greater portion of his skin. Some of the areas have grown pale, while others have deepened in color. He has had no loss of blood from any part of the body. He has continued his treatment of iron, arsenic, etc., up to within a few weeks. The physical examination shows a marked melanodermia of the face, neck, back, thorax, buttocks, elbows, pubic region, inner surface of the thighs, knees, and ankles, the pigmented patches being arranged somewhat symmetrically, with lighter vitiliginous areas between. (A fuller report of the condition of vitiligo shown by this case will be made elsewhere.) Otherwise the physical signs were about as before. The blood examination, made on January 7th: blood thin,

watery, and coagulates slowly. Marked poikilocytosis; 1 nucleated red cell (degenerating normoblast) to 150 leucocytes. Red blood cells, 874,400; leucocytes, 2546; hæmoglobin, 25 per cent.; specific gravity, 1029.

The patient's condition became worse quickly. On the 8th small hemorrhagic spots appeared over the thorax and extremities. On the 10th his dyspnœa and sweating had increased; there were moist râles over both lungs, mind clouded, pulse very rapid, low tension. Died at 9.03 A.M., January 10, 1900.

Clinical Diagnosis. Progressive pernicious anæmia; vitiligo. Autopsy held at 11.30 A.M., January 10th, by Dr. Warthin.

Autopsy Protocol. Body well built, 171 cm. long. Muscles small, emaciated, very flabby; on section pale-brownish-red, moist. Panniculus in small amount; on section bright golden-yellow. Slight œdema over lower extremities. Skin over the greater portion of the body is pale, slightly scaly, and inelastic. Over the lower part of the femurs, patellas, flexor surfaces of both knees; over the penis, inner surfaces of the thighs, flexor surfaces of the thighs and arms; over the buttocks, shoulders, and thorax, there are irregular patches of brown pigmentation, arranged somewhat symmetrically. Alternating with these there are areas of lighter, smoother skin. In the majority of the patches there is an abrupt change from the pigment to the light areas, the edge of the pigmented portion just next to the light skin appearing much darker. The pigmented patches have a concave margin toward the light areas. In a few places there is an intermediate lighter zone between the darkest pigmentation and the white skin. Over the legs and trunk there are sparsely scattered ecchymoses, varying in size from a pin-point to half a pea. Hair is scanty and white over the head and face. The body hair is entirely absent over the white areas.

Brain and spinal cord very anæmic, otherwise negative.

Diaphragm at fifth rib, right and left. Mediastinal fat in large amount, bright yellow. Small amount of clear fluid in each pleural cavity. On the right side there are numerous small ecchymoses in the parietal pleura. Apex in fifth intercostal space, inside the nipple line; 150 c.c. of clear fluid in the pericardial sac. Pericardium negative. Large, irregular, tendinous spots on the anterior and posterior walls of the right ventricle. Heart weighs 416 grammes. Subepicardial fat increased; œdematous. Numerous small ecchymoses beneath the epicardium of auricles. Auricles filled with thin, watery blood; no clots. Ventricles not dilated. Left ventricle hypertrophic, cavity small, the papillary muscles hypertrophic, and the chordæ tendineæ thickened. Throughout the myocardium there are small fibroid areas. Tricuspid and mitral rings slightly thickened; mitral flaps thickened and slightly retracted. Aortic valves slightly thickened, edges recurved. Pulmonary valves negative. Arterio-sclerosis in the beginning of aorta. Coronary vessels sclerotic and calcified.

The left lung is free throughout, voluminous, especially the lower lobe. Visceral pleura smooth, moist, clear, shining. Beneath it are about a dozen firm elevations the size of a pea, heavily pigmented, and on section show calcification. Apex is slightly retracted. Several small, airless areas felt throughout lung. On section the upper lobe is pale gray, anthracosis moderate. Pressure yields an abundant foamy exudate. Lower lobe shows marked hypostasis. Foamy exudate

without pressure. The right lung is free except at apex, where there are many small, irregular adhesions containing adipose tissue. Lung not so voluminous as the left. Slight hypostasis in the lower lobe. Pleura smooth, clear, and shining; contains a few calcified nodules the size of a pea. Apex slightly retracted; contains small, caseating tubercles, and a number of smaller, non-caseating nodules. Cut surface yields abundant exudate on slight pressure, but œdema is not so marked as in the left lung. Pulmonary vessels negative. Bronchi contain grayish-yellow fluid. Bronchial glands heavily pigmented; contain small calcified nodules.

Thoracic aorta shows patches of sclerosis, not longitudinally arranged. Thoracic duct negative. Œsophagus contains a small amount of yellowish, foamy mucus; mucosa pale. Mucosa of the mouth and upper respiratory tract very pale. Thyroid small, on section negative. Cervical lymph glands not enlarged, but the majority heavily pigmented, deep brown.

No fluid in the peritoneal cavity. Omentum rich in fat. Spleen weighs 224 grammes, 12 cm. long, 8 cm. broad, 4 cm. thick. Capsule irregularly thickened; shows numerous hyaline, pearly, nodular thickenings. On section, is pale brownish-red. Stroma greatly increased. Pulp decreased, soft; follicles not visible. Bleeds freely; vessels contain thin, watery blood.

Left adrenal measures 5.5 cm. x 2.5 cm. x 2 mm.; right, 4.5 cm. x 2.5 cm. x 2 mm.; the periadrenal tissue shows no inflammatory thickening. Bloodvessels and plexus on both sides apparently normal. No inflammatory tissue about the semilunar ganglia. On section, adrenals show beginning post-mortem change in the lower portions of the medulla, the medullary substance in the upper part of both organs being grayish-white, firm, and showing no brown pigmentation.

The left kidney weighs 192 grammes and measures 11 x 6.5 x 2.5 cm.; the right one weighs 176 grammes and measures 11.5 x 5 x 3 cm. Fatty capsules of both kidneys well developed; fibrous capsule strips off easily. Surface slightly granular. On section, both kidneys are pale brownish-red, firm. Medullary pyramids pale. Cortex of left measures 6 mm.; of right, 8 mm. Pelvic fat in large amount. Mucosa of pelvis negative. Ureters negative. Wall of bladder thickened, muscle trabeculæ hypertrophic. Small hemorrhage at base of the bladder.

The stomach contains 300 c.c. of greenish-yellow fluid, with much whitish mucus. Mucosa covered with grayish mucus. In the mucosa there are numerous ecchymoses of small size. Mucosa atrophic. Pylorus negative. No post-mortem change in the stomach mucosa. Intestine contains soft, bile-stained fecal material. Mucosa swollen, very pale, containing small punctate hemorrhages. Numerous enlarged solitary follicles in ileum. Large intestine contains soft, pale yellowish feces. Mucosa very pale, containing small hemorrhagic spots and small areas of pigmentation. No free blood in any portion of the intestinal lumen. Small hemorrhoids just within the anus.

The liver weighs 1728 grammes; its greatest dimensions are 25 x 17 x 7 cm. The surface is granular; capsule thickened, especially about the ligaments and near the gall-bladder. On section, the surface is granular, slightly elevated, cloudy, and of a pale red chocolate color. Slight fatty smear on knife. Outlines of lobules distinct; central vein

a small red point. Glisson's capsule slightly increased. Bile-ducts dilated, filled with golden-yellow bile. On the under surface of the liver is a small, triangular anomalous lobe of liver tissue entirely separated from the tissue of the main organ by connective tissue. Its capsule is thickened and shows lines of contraction. Gall-bladder and bile vessels negative. Portal vein is also negative.

The pancreas weighs 136 grammes; its dimensions are 24 x 4.5 x 1.5 cm. The tail is unusually thick. On section, the lobes are clearly outlined; interlobular connective tissue increased; consistency normal. The splenic artery and branches are very sclerotic.

The mesentery is very rich in fat, its glands slightly enlarged. On section, pale pink. The retroperitoneal glands are also enlarged, and are heavily pigmented, brownish-red in color. The glands at the brim of the pelvis in particular show this change.

The prostate shows bilateral enlargement, the testicles slight fibroid change; otherwise the genitals are negative.

Bone Marrow. Red marrow deep red in color. The fatty marrow of the long bones contains dark reddish areas looking somewhat like blood clots. The peripheral lymph glands are very slightly enlarged; all more or less pigmented. Near the solar plexus a number of enlarged Pacinian corpuscles are found, having pearly centres and a clear periphery.

Microscopic Examination. Lung shows anæmia and marked œdema. Old and fresh hemorrhagic infarcts. Mucopurulent bronchitis. Healed tubercles.

Heart. Atrophy and hypertrophy. Fatty infiltration and degeneration.

Spleen. Atrophy, increase of fine stroma, chronic congestion; contains very little hæmosiderin.

Kidneys. Anæmic; atrophy of cortex, with localized areas of connective-tissue increase. Numerous obliterated glomeruli. Cells of convoluted tubules show cloudy swelling, and contain a diffuse yellowish pigment which gives the iron reaction.

Liver. Atrophy, increase of connective tissue, slight fatty infiltration and degeneration; chronic congestion. Liver cells heavily pigmented with brownish pigment, most marked at the periphery of the lobule. The pigment gives the iron reaction.

Pancreas. Atrophy and increase of interlobular tissue. Some of the areas of Langerhans appear enlarged.

Adrenals. Slight atrophy and marked hæmosiderosis. Collections of deeply staining small round cells found throughout both organs; numerous mast cells present.

Stomach. Chronic atrophic gastritis; small hemorrhages in submucosa.

Intestine. Subacute enteritis and colitis. Solitary follicles and Peyer's patches enlarged and œdematous; some hemorrhagic.

Prostate. Adenomatous hyperplasia; numerous corpora amylacea.

Aorta. Marked sclerosis.

Skin. Melanoderma and vitiligo. Pigment does not give the iron reaction. (The vitiligo of this case will be reported elsewhere.)

Bone Marrow. Red marrow contains increased number of nucleated reds and megaloblasts. The red areas in the fatty marrow are localized areas of congestion and hemorrhage.

Hæmolymph Glands. See below.

Lymph Glands. All lymphatic glands show hæmosiderosis.

Pathological Diagnosis. Pernicious anæmia; hæmosiderosis of the liver, kidneys, lymph glands, adrenals, and spleen; vitiligo; chronic atrophic gastritis; acute enterocolitis; multiple punctiform ecchymoses; general atrophy; arterio-sclerosis; healed tubercles of the lungs and bronchial glands; small-celled infiltration of the adrenals; hypertrophy of the prostate.

CASE II.—Miss Sarah M., American, aged fifty-two years, housekeeper by occupation, was admitted to the medical clinic January 12, 1899. The patient came to the hospital because of shortness of breath, "jumping sensation" in the heart region, and general weakness. Her father died at the age of sixty-five years of a disease which the patient thinks was similar to hers. Otherwise the family history is unimportant. Patient had the usual diseases of childhood. There is a strong suspicion of syphilis. She has worked very hard; habits of eating have been very irregular. Menopause established three years ago. At this time she began to have pain and throbbing in the epigastrium after meals, and shortness of breath developed at the same time. Large "swellings" appeared on the face, lasting six to eight months. Her physician at this time said that her liver and spleen were very much enlarged. She improved under treatment, but six months later became much worse, being confined to bed for about four weeks. During this attack she several times, after meals, vomited a bloody looking material, which she described as "thick, livery matter." Four weeks ago the throbbing pain in the heart region and shortness of breath became much worse. She has been unable to sit up; mind not clear. During these attacks her skin is of a yellow color. During the last summer she gained forty to fifty pounds.

Physical Examination (January 13, 1899). Patient appears very ill, cachectic, mind clouded, very restless, face swollen; skin is very pale, sallow, and elastic. Slight œdema at the ankles. No enlarged glands. Examination of the lungs negative. Apex in fifth intercostal space, outside of the nipple line; heavy impulse with systolic thrill. Dulness enlarged to the left nipple line and to the right one finger's breadth beyond the right edge of the sternum. Loud, blowing systolic murmur over the entire cardiac region, loudest over the apex, and transmitted into the axilla. Second sounds weak. Pulse 112, low tension, somewhat dicrotic, irregular in volume and rhythm. Abdomen above the level of the ribs. Traube's space dull; lower border of the stomach two inches above the umbilicus. Liver dulness reaches to the edge of the ribs. Liver is palpable. Splenic dulness begins on the eighth rib and extends to the edge of the ribs. Spleen easily felt one to one and a half inches beyond the edge of the ribs.

Blood Examination (January 13, 1899). Red blood cells, 888,000; leucocytes, 4700; hæmoglobin, 35 to 40 per cent. Differential count (January 18, 1899): small lymphocytes, 33 per cent.; large lymphocytes, 7 per cent; transitionals, 1.8 per cent.; polynuclears, 56.2 per cent.; eosinophiles, 0.70 per cent.; degenerating leucocytes, 2.1 per cent. The red blood cells are large, as a rule; some microcytes, marked poikilocytosis. The cells are pale, with large, clear centres. Normoblasts, degenerating normoblasts, and megaloblasts are present.

There is a trace of albumin in the urine.

The patient failed very rapidly after admission. General weakness increased. Irregular fever; heart gradually became weaker; œdema of the legs increased. Died at 10 A.M., January 20, 1899.

Clinical Diagnosis. Pernicious anæmia; dilatation of the heart; relative mitral insufficiency.

Autopsy by Dr. Warthin, 11 A. M., January 20, 1899.

Autopsy Proctocol. Body well built, 159 cm. long. Muscles very soft and flabby; rigor mortis present only in the muscles of the jaw. Body heat present over the trunk. Panniculus very thin; on section, orange-yellow. Moderate œdema over lower extremities, slight œdema over the remainder of the body. Skin pale sallow, with a yellowish tint; numerous small, pigmented patches over both legs. Small ecchymoses in abdominal wall just below umbilicus. Small patch of ectatic veins on the outer surface of the right thigh. Slight hypostasis over back. Brain negative, except for anæmia and slight sclerosis of the cerebral vessels. Spinal cord not examined.

Diaphragm on the right at the third interspace; on the left at the fifth rib. Left mammary gland is negative; right one contains a small cyst. Position of the thoracic organs negative, except for the apex of the heart, which is in the fifth interspace in the anterior axillary line. Mediastinal fat abundant, bright yellow and moist. No remains of thymus.

Pericardial sac contains 100 c.c. of clear fluid. Pericardium pale, clear, shining. Large tendinous spot on the anterior wall, and smaller one on the posterior. Heart weighs 473 grammes, and is three times as large as cadaver's right fist. Subepicardial fat is increased. Beneath the epicardium there are numerous punctiform hemorrhages, the largest being at the apex. The apex is formed by the left ventricle. The right auricle is greatly distended, the muscle fibres separated. Right heart filled with thin, watery blood; no clots. Left side not dilated. Left ventricular wall measures 10 to 15 mm.; right, 2 to 5 mm. Mitral orifice barely admits two fingers; flaps thickened, posterior one shortened. Aortic flaps thickened, but adequate. Punctiform hemorrhages beneath endocardium. Heart muscle, pale yellowish-brown; soft; no sclerosis in the aorta.

Both lungs moderately collapsed, very pale, moderate anthracosis, moderate œdema. Small calcified nodules in the upper lobe of the left. Bronchi, bronchial glands, and pulmonary vessels negative. Upper respiratory tract negative except for extreme paleness of the mucous membranes. Tonsil contains a number of small scars. Small hemorrhage on the upper surface of the right vocal cord. Both lobes of the thyroid enlarged; in the left lobe there is an adenoma the size of a small pigeon's egg. Œsophagus, trachea, and thoracic duct negative. Cervical lymph glands enlarged, some of them showing anthracosis.

No fluid in the peritoneal cavity. Position of the abdominal organs negative. Omentum rich in fat; contains three small, firm, pinkish bodies, the largest the size of a bean.

The spleen weighs 570 grammes and measures 18.5 x 9 x 5.5 cm., about three times the normal size; edges thick and rounded. Capsule tense, thickened, and opaque. Cut surface is dark red; consistence firm, stroma increased, follicles enlarged, bleeds very little. Splenic vessels show marked sclerosis.

Adrenals negative; no post-mortem change.

Left kidney weighs 160 grammes and measures 12 x 4.5 x 4 cm.; right kidney weighs 146 grammes and measures 12 x 5 x 4 cms. Cortex of the left kidney, 0.5 cm. broad; that of the right a little less. Fatty capsule of both kidneys very large; fibrous capsule thickened and slightly adherent. Surface granular—that of the right more so than the left. Cut surface is pale brownish-red, slightly granular; consistency increased. Small, grayish areas in the cortex; waxy shine. Glomeruli plainly visible. Pelves and ureters negative. Bladder distended with clear urine; walls thin and pale. Stomach shows no post-mortem change. No atrophy or other pathological change. Contains about 500 c.c. of greenish fluid in which there is a whitish powder. Intestines filled with soft, greenish, fecal material. Mucosa pale, otherwise entirely negative. Appendix normal.

Liver weighs 2105 grammes and measures 30 x 23 x 10 cm. Lower edge is three finger breadths below the edge of the ribs, in the right nipple line. Left lobe is lengthened and flattened. On its upper surface is a depression corresponding to the position of the heart. Numerous adhesions over the anterior surface. Capsule thickened, especially near the ligaments. On section the organ is brownish-yellow; lobules not clearly defined, very little blood in the veins. Slight fatty smear on knife. Consistence increased. Gall-bladder distended and filled with dark brown, glairy bile; wall thin; bile passages and portal vein negative. Pancreas large; marked fatty infiltration. Vessels sclerotic. Three enlarged glands behind the pancreas; on section, pinkish-brown. The mesentery is very rich in fat; the mesenteric glands not enlarged. The retroperitoneal glands are not enlarged; many of them are pinkish or brownish in color. The abdominal aorta shows a moderate degree of sclerosis.

External genitals negative. Vagina negative. Cystic polypoid growth on the cervix. Cystic endometritis. Uterine wall atrophic. Left tube twisted, bent upon itself, surrounded by many adhesions; few adhesions about the right tube. Ovaries atrophic, the left one bound down by adhesions. Uterine ligaments thickened, show many adhesions; also adhesions between the uterus, ovaries, and the rectum.

Marked osteoporosis of the long bones; the medullary canal of the right tibia about twice the normal size. Marrow, bright red; no fatty marrow in the long bones. Hyperplasia of red marrow in the clavicle, etc.

The peripheral glands are not enlarged; negative.

Microscopic. Spleen. Fibroid hyperplasia; moderate hæmosiderosis.

Liver. Atrophy, fatty degeneration, hæmosiderosis of the peripheral zone of lobule, chronic endarteritis in hepatic artery.

Kidneys. Early stage of primary contracted kidney, chronic endarteritis, hæmosiderosis of convoluted tubules.

Pancreas. Fatty infiltration.

Lungs. Atrophy, œdema.

Heart. Atrophy, fatty degeneration, and infiltration.

Adenoma of Thyroid. Adenoma showing large myxomatous areas partly infiltrated with red blood cells.

Stomach and Intestines. Negative.

Bodies from Omentum. Hæmolymph glands showing pigmentation and active hæmolysis.

Bone Marrow. Fatty marrow transformed to lymphoid marrow containing many nucleated red cells.

Retroperitoneal Glands. See below.

Pathological Diagnosis. Pernicious anæmia; hæmosiderosis of the liver, spleen, kidneys, and hæmolymph glands; hyperplasia of the lymphoid marrow; fibroid hyperplasia of the spleen; general atrophy, fatty infiltration, and degeneration of the heart; cardiac dilatation; mitral insufficiency.

CASE III.—Mrs. H. E., aged fifty-eight years, American, housewife, was admitted to the medical clinic November 24, 1900. Patient comes to the hospital for general weakness, shortness of breath, and frequent hemorrhages from the nose, gums, and bowels.

Family history negative; previous history good. Has always been a very hard worker. Menopause began at forty-three years; flowed excessively at intervals up to the age of fifty-one years, when the flow suddenly ceased. The present trouble began a year from last August, when she contracted a severe cold, became very constipated and weak. Two months later she fell and struck her forehead. Six days later she had a severe epistaxis, lasting six hours. A month later she had another attack of epistaxis, of eight hours' duration. Periodical attacks of nose bleeding occurred every month until the following spring, the epistaxis continuing for seven to ten hours without apparent ill effects. For seven weeks previous to last May she was free from hemorrhage, but in May began to have hemorrhages from the nose and gums, continuing more or less for six weeks. During the greater part of this time she was confined to her bed, extremely weak, nauseated, and retained food with great difficulty. In July she had an epistaxis of thirty-six hours' duration. Slight one during August. In September she had another severe attack, and vomited a great deal of blood; cannot say whether the blood came from the stomach or nose. During the middle of October she had almost constant, though not profuse, hemorrhages from the nose, gums, and lips. During the last two weeks these have ceased, but she has had a bloody diarrhœa, the blood coming in a steady stream at times and apparently unchanged. During the period of hemorrhage she is very weak; staggers in walking, but has lost consciousness only once. Elastic swellings have appeared in various parts of her body, the first and largest, the size of two fists, on the right shoulder, gradually working down the right side to the right hip, where it ultimately disappeared. A similar mass on the left arm became harder. The skin over the abdomen became discolored, the discoloration gradually disappearing. Sight has become dim. Appetite remains good; has lost fifty pounds. Irregular fever.

On December 7th patient became comatose, but could be aroused easily. Face was very œdematous; marked œdema at the ankles. Pulse 110; low tension. Later in the day the coma deepened and breathing became more labored. Died suddenly at 5 A.M. December 8th.

Blood Examination. Red blood cells, 1,280,000; leucocytes, 3000 to 4000; hæmoglobin, 20 per cent. The differential count of 500 leucocytes showed: small lymphocytes, 40.4 per cent.; large lymphocytes, 3.3 per cent.; transitionals, 2.2 per cent.; polynuclears, 53.6 per cent.; eosinophiles, 0.4 per cent.; degenerating leucocytes, 0.2

per cent. One normoblast in two smears. (Smears given to the blood class in the pathological laboratory showed in some covers two to three megaloblasts and the same number of degenerating normoblasts.) The blood showed evidences of an extremely active hæmolysis. The red cells were nearly all round, some dark, many pale or shadowy. The plasma showed a tendency to stain around the red cells. The red cells are grouped two or three or more in a bunch. No particular changes in the leucocytes.

Clinical Diagnosis. Anæmia (active hæmolysis); hæmophilia.

Autopsy performed by Dr. Warthin, at 11.45 A.M., December 8th, at undertaking shop.

Autopsy Protocol. Body five feet six and a half inches tall; well built; abdomen distended above the level of the ribs; punctured by the undertaker. Muscles small and flabby; on section, very pale and soft. Rigor mortis present throughout. Panniculus in fair amount; on section, orange-yellow, moist. Skin dry, inelastic, pale sallow, with yellow tint. Numerous small pigmented nævi scattered over the body. Several angiectatic areas or subcutaneous hemorrhages. Over the forearm, face, neck, external genitalia, and knees the skin is moderately pigmented, the pigmentation less marked over the flexor surfaces. Mucous membranes pale yellow. Scleræ very slightly yellow. Pale hypostasis over the back. Hair of the scalp abundant, grayish. Marked œdema over the lower extremities; slight over the thorax. Body heat absent.

Head and spinal cord not examined.

Diaphragm, fifth rib on right; sixth intercostal space on left. Mammæ atrophic. Position of the thoracic organs normal. Mediastinum negative. Thymus fat in small amount. Pleural cavities filled with fluid smelling of undertaker's injection. Pleuræ negative. Pericardium negative. Heart larger than the right fist; weighs 186 grammes. Small, tendinous spot on the posterior wall of the right ventricle; no subepicardial ecchymoses. On section, heart muscle is pale brownish-red in color; subepicardial fat greatly increased. Left ventricle wall 12 mm. thick; right, 5 mm. Valve flaps and orifices negative. Both lungs entirely free; the right one partly collapsed, the left more voluminous. Pleuræ negative. On section, both lungs are pale pinkish-gray in color; yield abundant foamy exudate on slight pressure, emphysematous along the edges and at the apices. Pulmonary vessels negative. Bronchi empty; mucosa pale. Bronchial glands moderately enlarged, moderately pigmented. Arch of the aorta and thoracic aorta show beginning arterio-sclerosis. Upper respiratory tract negative. Thyroid enlarged; contains hyaline and calcified areas; cyst the size of a cherry in the lower part of the left lobe. Thoracic duct negative. Œsophagus negative.

Liver two hand breadths below the ensiform and a hand breadth below the edge of the ribs; otherwise the position of the abdominal organs is negative. The omentum is rich in fat, rolled up at the level of the umbilicus. Peritoneum negative; in the serosa of the small intestine there is a number of small, hyaline thickenings. No fluid in the peritoneal cavity.

Spleen weighs 208 grammes: about normal in size and shape. Notches on the anterior margin well marked. Capsule slightly thickened and wrinkled. Consistency soft. On section, the pulp is bluish-red,

stroma slightly increased, follicles somewhat diminished in number, but of fair size.

The adrenals show post-mortem change; otherwise negative. The left kidney weighs 240 grammes; the fatty capsule well developed. Kidney more plump than normal; fibrous capsule thickened and slightly adherent. Numerous retention cysts in the surface of the cortex, varying in size from a pin-head to a pea. On section, the surface is slightly granular, pale, firmer, and more translucent than normal. Labyrinth and medullary rays not well marked. Glomeruli not easily seen. Cortex measures ½ to 1 cm. Pelvic fat increased. The right kidney weighs 256 grammes; similar to the left, except that the lower pole is almost entirely replaced by a large retention cyst, having a clear wall, almost transparent, and containing clear fluid. In the upper pole there are other similar cysts of the size of a cherry. Both ureters dilated, the left more than the right. Mucosa pale, otherwise negative. Bladder greatly distended; wall smooth.

Stomach contains food remains and a small amount of mucus. Mucosa swollen; no evidences of atrophy. Mucosa of the small intestine very pale, otherwise no change. Neither the solitary follicles nor Peyer's patches enlarged. Appendix long, slender; has long mesentery, very rich in fat; no adhesions. Cæcum moderately dilated. Ascending colon empty; mucosa covered with mucus. Ascending colon contains pale yellowish unformed feces. Mucosa shows little change. Transverse colon is contracted; mucosa covered with tenacious mucus and small fecal lumps; no evidences of hemorrhage. Descending colon empty. Mucosa covered with a large amount of mucus; mucosa pale, thickened, no evidences of hemorrhage. Above the anus there is a ring of large, dark-blue, tortuous hemorrhoids. No evidences of recent hemorrhage from these.

The liver weighs 1920 grammes; much flattened, its sagittal diameter increased. Over the lower border of the right lobe, corresponding to the edge of the ribs, there are two shallow furrows, one-half finger breadth in width, over which the capsule is much thickened and opaque. The surface of the liver is more or less irregular, especially that of the left lobe and the under surface of the right one. The capsule is thickened throughout; more marked thickening over the depressions and furrows. Consistency decreased. On section, shows a well-marked nutmeg appearance; central portion of lobule deep red, peripheral brownish-yellow. Marked fatty smear. Gall-bladder filled with dark golden-brown bile; mucosa negative, wall somewhat œdematous. Bile passages patent.

Pancreas very small, flattened, consistency decreased. On section, lobules small and pale. Fat about the pancreas in large amount. No hemorrhage. Portal vein negative. Mesenteric glands not enlarged. Retroperitoneal lymph glands enormously enlarged, forming large, flattened masses lying along the vessels on both sides of the spinal column from the bifurcation of the common iliac to the solar plexus. Enlargement more marked on the right side than on the left. Glands around the solar plexus very large and firm. The glands are partly dark red, partly pale, showing a number of dark-red areas; consistency soft; cut surface somewhat granular; the scraping yields a large number of cells. Vessels greatly dilated and filled with thin blood.

The external genitals are pale; labia somewhat œdematous. Cervical

ectropion. Uterus enlarged, thick; irregular increase in size due to a number of myofibromata in the wall, from the size of a cherry to a walnut; tubes atrophic. Ovaries small and atrophic; show many hyaline scars. The right broad ligament is studded with numerous small hyaline bodies, the majority translucent and slightly yellow. Some are firm, others cystic; they vary in size from a pin-head to a small pea.

Red marrow dark red. Long bones show marked osteoporosis; medullary canal greatly enlarged, the fatty marrow replaced by dark red to almost black lymphoid (?) marrow containing small cysts filled with dark-red fluid blood. The firm portion of the bone forms a very thin shell around the canal, and is much softer than normal. Peripheral lymph glands not enlarged.

Microscopic. Heart. Shows marked atrophy, fatty infiltration, and moderate fatty degeneration.

Lungs. Very marked simple atrophy and emphysema and dilatation of the smaller bronchioles.

Spleen. Atrophy and chronic congestion; moderate hæmosiderosis.

Liver. Marked chronic congestion (nutmeg liver); slight hæmosiderosis of the peripheral zone of the lobules.

Kidneys. Early stage of chronic interstitial nephritis; numerous retention cysts; slight hæmosiderosis of the convoluted tubules.

Pancreas. Fatty atrophy, congestion, beginning post-mortem change.

Stomach. Chronic catarrhal gastritis, moderate atrophy.

Intestine. Negative.

Ovaries. Atrophy.

Cysts from Broad Ligament. Follicular cysts lined with large flattened or cuboidal cells; contain a mucoid or firm colloid substance.

Skin. Small hemorrhagic areas.

Bone Marrow. Contains many hemorrhagic areas and small, scattered islands of lymphoid marrow, these being made up chiefly of lymphocytes and numerous giant cells. Cysts, containing fresh blood.

Lymph Glands. See below.

Pathological Diagnosis. Anæmia gravis; active hæmolysis; lymphoid hyperplasia of the retroperitoneal glands lymphosarcoma (?), infective granuloma (?), early stage of leukæmia (?); lymphoid and cystic changes in the bone marrow; fatty heart; atrophy, chronic congestion of the spleen, lungs, liver, etc.; early stage of chronic interstitial nephritis; myofibromata of the uterus; multiple ecchymoses in the skin.

Case IV.—W. M., aged twenty-two years, American, laborer, admitted to the medical clinic January 25, 1901. His family history is unknown. At twelve years of age he had an attack of "jaundice," lasting two weeks; otherwise has had fair health. He entered the army service April 29, 1898, and was sent to Porto Rico, where he almost immediately contracted malaria and chronic diarrhœa. Was discharged April 14, 1899; has not been well since. Has four to five stools daily; these are thin, watery, and passed with much gas and more or less pain. He has great thirst; drinks an average of two gallons daily; passes about one gallon of urine during the night, does not know how much during the day. Complains of great general weakness, constant pain in the lumbar region, and at times swelling of the extremities and face.

Physical Examination. Weight, 93¾ pounds. Very cachectic and emaciated. Skin and scleræ of a muddy tint; pigmented patches over the neck and spine. Examination of the lungs negative. Heart sounds weak; soft, blowing systolic murmur at the apex. Pulse rapid; low tension. Has irregular, low fever. No enlargement of the spleen, liver or lymph glands. Specific gravity of urine, 1003; chemical tests negative. Examination of the stools showed no protozoa, no worms or eggs, no blood, many leucocytes.

Blood Examination. Red blood cells, 960,000; leucocytes, 3172; hæmoglobin, 20 per cent.; specific gravity, 1027. Red cells show marked poikilocytosis; stain very poorly; few degenerating normoblasts.

The patient rapidly became very weak, attacks of faintness occurring. Died 8.30 A.M., January 29, 1901.

Clinical Diagnosis. Anæmia; chronic diarrhœa.

Autopsy by Dr. Warthin, 4 P.M., January 29, 1901.

Autopsy Protocol. Body measures 170 cm.; much wasted and cachectic. Muscles emaciated, very flabby; on section, brownish-red, dry; do not tear easily. Rigor mortis present throughout. Panniculus almost entirely absent. On section, pale orange-yellow, dry. Trace of œdema over the lower extremities. Skin dirty sallow; marked pigmentation in axillæ, around the nipples, over the abdomen, genitals, and thighs. Numerous small, pigmented moles scattered over the body; pigmented patch over the eighth rib, in the right anterior axillary line. Very slight pale hypostasis over back. Body heat present over the abdomen and lower part of the thorax. Body hair scanty; scalp hair dry and thin.

Brain and cord very anæmic; otherwise negative.

Diaphragm, fourth rib on right; fifth intercostal space on right. Apex in the fourth interspace, half-way between the left parasternal and nipple lines. Mediastinal fat in small amount; no enlarged glands. Thymus fat in small amount; no remains of thymus. Small amount of cloudy, yellowish fluid in both pleural sacs.

Pericardial sac moderately distended; contains 75 c.c. of pale yellow, slightly cloudy fluid. Parietal pericardium negative. Epicardium clear, shining, moist; a few small ecchymoses beneath the epicardium of the right auricle. Heart weighs 304 grammes; size of cadaver's right fist; soft; subepicardial fat in slight excess. On section, heart muscle is pale brownish-yellow, soft, tears easily. Right auricle and vena cava distended with thin, watery blood and large yellow agonal clot. Left auricle divided into a number of anomalous narrow lobules, slightly recurved on themselves. Left ventricular wall measures 10 mm.; right, 3 mm. Slight thickening of the proximal margins of the mitral flaps; otherwise the valves and orifices are negative.

Left lung entirely free, moderately voluminous. Pleura negative. On section, lung is extremely pale, almost bloodless; slight foamy exudate obtained by pressure. Right lung free, except for a tough band of adhesions at apex containing a calcified nodule. On section, similar to the left. Pulmonary vessels negative. Mucosa of bronchi pale. In the right peribronchial glands is a number of caseous and partly calcified areas. Thoracic duct negative. Mucosa of the upper respiratory tract very pale. Left tonsil enlarged; suppurating crypt. Left lobe of the thyroid moderately enlarged.

In the right side of the neck, along the anterior border of the sterno-cleidomastoid and just below the angle of the jaw, there is an elastic, lobulated body, about 4 cm. long by 2 cm. wide. Skin over the mass is pigmented, but freely movable; there is no external opening. On section, presents the appearance of fat tissue.

Small amount of clear yellow fluid in the peritoneal cavity. Omentum contains a small amount of fat; very anæmic; lower edge rolled to level of the umbilicus. Intestines uniformly distended; walls thin, dry, bloodless. Sigmoid flexure greatly distended, completely filling up the pelvis and inguinal regions. Colon also greatly distended.

Spleen weighs 240 grammes; somewhat enlarged, flattened, soft; anterior notches small. Near the upper pole there is a deep posterior notch. Capsule is slightly wrinkled. On section, the pulp is swollen, covering up the stroma; mottled pale red and darker red. Follicles easily seen.

Adrenals negative. Left kidney weighs 296 grammes; right, 240 grammes. Fatty capsule of both rather poor in fat; fibrous capsule slightly adherent. Both kidneys plumper than normal, surfaces slightly granular, consistency increased. On section, parenchyma very pale and firm; outline of labyrinth and medullary rays not very distinct; glomeruli barely visible. Medullary pyramids pale, glistening, almost white. Iodine test for amyloid negative. Pelves dilated; ureters greatly dilated. Bladder enormously distended; filled with pale urine. Mucosa pale, smooth.

Mucosa of stomach very pale, otherwise negative. In the ileum there are scattered erosions over enlarged solitary follicles. These increase in number and size toward the ileocæcal valve. In Peyer's patches are several small ulcers, the largest 15 mm. long and 5 mm. wide. Ulcers are excavated; have overhanging thickened margins; base covered with gray exudate; do not extend through the submucosa; are longitudinal and not circular. Serosa shows no change. No ulcers in the colon. Rectum negative.

Liver weight, 1792 grammes; rounder than normal; capsule negative. On section, color pale yellowish-brown; central veins congested, pale red. Surface cloudy; slight fatty shine and smear. Gall-bladder contains pale golden-yellow bile; negative. Bile passages normal.

Pancreas extremely pale; outlines of lobules sharply marked.

Mesenteric glands moderately enlarged; on section, pale, homogeneous; no necrosis.

Retroperitoneal hæmolymph glands greatly enlarged, especially on the right side of the spine, behind the vena cava, along the abdominal aorta, and near the left renal artery. Glands are of a deep brown color. Glands about the solar plexus are also enlarged and of a brown color, although not so dark as the hæmolymph glands.

With the exception of a large varicocele on the left side and thickening of the testicular tunics, the genitals are negative.

Bone marrow: Red marrow bright red; fatty marrow pale, shows no lymphoid areas in the long bones of the lower extremities.

Peripheral lymph glands negative.

Microscopic. Heart. Simple atrophy.

Lung. Atrophy; hemorrhagic infarction.

Bronchial Glands. Old, calcified tubercles.

Tonsils. Chronic tonsillitis.

Tumor from Neck. Lipoma.

Liver. Simple atrophy; slight fatty change; slight hæmosiderosis of the peripheral zone of lobule.

Spleen. Congestion; hyperplasia of pulp.

Kidneys. Atrophy; dilatation of tubules; slight hæmosiderosis of cells of convoluted tubules.

Adrenals. Pancreas and thyroid negative.

Intestinal Ulcers. Tuberculous (?).

Mesenteric Glands. One gland contains a number of tubercles showing caseation and large giant cells.

Hæmolymph and Retroperitoneal Glands. See below.

Bone Marrow. Red marrow shows a great number of normoblasts and megaloblasts. Fatty marrow shows no lymphoid change.

Pathological Diagnosis. Pernicious anæmia (?); tuberculous ulcers of the intestine; tuberculosis of the mesenteric and bronchial glands; acute congestion of the spleen; general marasmus and atrophy of all the organs; lipoma of the neck.

CASE V.—O. D. C., aged twenty-five years, American, farmer, admitted to the medical clinic January 20, 1901. Comes to the hospital because of diarrhœa, gastric disturbances, shortness of breath, and yellowness of the skin. Family history negative. Had frequent "fits" when a baby; was not strong as a boy; had several attacks of vomiting. Habits good. In February, 1898, had an attack of "grippe," since which time he has not been well. Has had frequent attacks of nausea and pain in the stomach, in which he vomits; is better after vomiting. Under treatment with arsenic he became better, but is at present so weak that walking is fatiguing. Is troubled with palpitation. Has two to three loose, watery stools a day; no blood in the stools. Of late this condition has been improving. During attacks has sore mouth, fever, frontal headache, and feeling of numbness over the entire body. Has no appetite.

Physical Examination. Cachectic, but not emaciated; mind is clear. Muscles small and soft. Fair amount of panniculus. Skin is light yellow; mucous membranes very pale. Scleræ contain yellowish fat; no jaundice. No enlarged glands. Examination of the lungs negative. No apex-beat. Heart dulness not enlarged; first sound impure. Over pulmonary area there is a short, soft, blowing, systolic murmur. Pulse 88, regular, of low tension. Splenic dulness enlarged; spleen not palpable. Liver dulness not enlarged. Succussion in the stomach. Urine contains albumin and casts. No blood, mucus, parasites, or eggs in the stools.

Blood Examination. Red cells, 1,600,000; leucocytes, 4413; hæmoglobin, 35 to 40 per cent.; specific gravity, 1040. Red cells show marked poikilocytosis; no nucleated red cells found.

The patient remained in the hospital until March 7th. Improved greatly; hæmoglobin rose to 60 per cent. He was allowed to take medicine (iron, hydrochloric acid, etc.) and to go home, returning in a few months for further examination.

He returned April 17th, neither looking nor feeling so well as when he left. Has increased shortness of breath, loss of appetite, irregular fever; skin is more yellow. Red cells, 1,828,000; hæmoglobin, 40 per cent. From this time on he gradually grew weaker, with short periods of apparent improvement. Attacks of nausea, vomiting, and præcordial

pain became frequent; a number of attacks of nosebleed occurred. Red cells and hæmoglobin steadily went down, the blood count on May 3d being: red cells, 766,000; leucocytes, 8567; hæmoglobin, 35 to 40 per cent. Red cells showed marked poikilocytosis; degenerating normoblasts and megaloblasts present.

Died May 15, 1901, at 4.15 A.M.

Clinical Diagnosis. Pernicious anæmia.

Autopsy by Dr. Warthin, 9 A.M., May 15, 1901.

Autopsy Protocol. Body 167 cm. long; no anomalies or deformities. Abdomen below the level of the ribs. Muscles small, soft, and flabby; on section, pale brownish-red. Small amount of panniculus; on section, light lemon color. Slight œdema over the lower extremities. Rigor mortis present throughout. Body heat present in slight amount over the thorax and abdomen. Skin and scleræ of a dirty lemon color. Genitals are heavily pigmented; darker pigmentation on the under side of the penis. Skin over the abdomen and flexor surfaces darker than elsewhere. No hypostasis.

Inner surface of the skull-cap much eroded and roughened. Dura adherent over convexity, and thicker than normal. With the exception of extreme anæmia, brain and spinal cord are otherwise negative.

Diaphragm at sixth intercostal space on the right; sixth rib on the left. Position of thoracic organs negative. Examination of the mediastinum negative. No remains of the thymus. No fluid in the left pleural cavity; small amount in the right. Left pleura covered with small, delicate adhesions; right pleura smooth and shining. Pericardial sac distended. Pericardium negative. Subepicardial fat in excess.

Heart weighs 322 grammes; somewhat smaller than cadaver's right fist. Cavities contain pale, watery blood. Heart muscle very pale, brownish-yellow, very soft, tears very easily. Thickness of the left ventricular wall, 10 to 12 mm.; of right, 2 to 3 mm. of muscle, and 1 to 2 mm. of fat. Slight thickening of the proximal surfaces of the flaps; otherwise valves and orifices are normal.

The left lung weighs 490 grammes. It is adherent throughout by delicate, easily torn adhesions. Voluminous. On section, extremely pale. Slight hypostasis in the posterior portion of the lower lobe. On pressure, yields an abundant foamy exudate. Very slight anthracosis. Right lung weighs 360 grammes; entirely free; otherwise similar to the left lung. Mucosa of the bronchi extremely pale; they contain grayish, foamy fluid. Pulmonary vessels and bronchial glands negative. Mucosa of the œsophagus very pale. Thoracic duct and great vessels of the thorax negative. In the posterior mediastinum three small, deep-red glands were found (hæmolymph glands?).

Mucous membrane of the upper respiratory tract very pale. Teeth very poor. Thyroid very small; weighs 20 grammes. Two parathyroids on the left side, one larger one on the right side; all three very brown. In the deep cervical region about thirty small glands, the size of a pea or larger, red to deep bluish-red in color, were found (supposed hæmolymph glands).

Peritoneal cavity contains 1 litre of clear fluid (undertaker's injection). Liver two finger breadths below the edge of the ribs, in the right nipple line. Colon is distended; lies below the level of the umbilicus. Position of the abdominal organs otherwise negative. Omentum very rich in pale lemon-colored fat.

The spleen weighs 126 grammes and measures 11.5 x 7 x 3 cm. Rather flat; kidney-shaped. The poles curve anteriorly much more than normally. On the anterior edge are several deep notches; one very deep one near the upper pole. Capsule is thickened, and near the upper pole is covered with fine, stringy adhesions. On section, the pulp is a light brownish-red color; consistency firm; stroma relatively increased; follicles decreased in number and size. Very pale, watery blood in the larger vessels.

The left kidney weighs 140 grammes and measures 10.5 x 5 x 3 cm. The fatty capsule is moderately rich in pale yellow fat. The fibrous capsule strips off easily. Surface very pale; venæ stellatæ barely visible. On section the surface is very pale, moist, and shining. Pelvic fat increased. The right kidney weighs 156 grammes and measures 10 x 4 x 2.5 cm.; in all respects similar to the left. Both adrenals negative. Ureters and bladder negative.

The stomach is moderately distended; strong odor of H_2S on opening. Contains a small amount of bile-stained fluid. Walls very thin; mucosa very atrophic, covered with bile-stained mucus. Punctiform hemorrhages scattered throughout the mucosa. Mucosa of the duodenum very pale. About the middle of the ileum there is a small, superficial ulcer, apparently almost healed. Appendix negative. Large intestine contains pale formed feces. Mucosa very pale.

The liver weighs 1736 grammes; greatest dimensions, 34 x 18 x 7.5 cm. Capsule slightly thickened about the ligament. On section, very anæmic; light chocolate color; lobules distinctly outlined; central portion of lobules paler than peripheral, and slightly elevated; has "cooked" appearance. Gall-bladder adherent to the duodenum and pylorus by easily torn adhesions; distended with dark brownish bile. Bile passages patent. Portal vein negative.

Pancreas negative. Near its tail is a small body the size of a pea, pale brown in color, resembling the spleen.

The mesenteric glands are not enlarged; appear normal.

About fifty small glands, the largest the size of a bean, all red or bluish-red in color, taken from the retroperitoneal region.

Penis and scrotum deeply pigmented; testicles very small and soft; otherwise examination of the genitals negative.

The peripheral lymph glands are not enlarged and present no unusual appearance. Fatty marrow of the long bones contains lymphoid areas. Marked osteoporosis.

Microscopic. Heart. Atrophy and fatty degeneration.

Lungs. Œdema and a number of old, hemorrhagic infarcts.

Spleen. Atrophy, fibroid hyperplasia, chronic congestion, hyaline change in the walls of vessels, very slight hæmosiderosis.

Kidneys. Marked hæmosiderosis of the cells of the convoluted tubules.

Stomach. Atrophic catarrhal gastritis.

Pancreas. Slight atrophy.

Liver. Atrophy and fatty degeneration, the latter process being most marked in the central portion of the lobules. Marked hæmosiderosis of the peripheral zone of the lobules.

Marrow. Fatty marrow from the tibia contains a few points of red marrow.

Red Marrow. Megaloblastic in character.

Lymph Glands. No change in the ordinary lymphatic glands; one gland from the cervical region showed an apparent great increase in the number of bloodvessels, the walls of these being greatly thickened.

Hæmolymph Glands. See below.

Pathological Diagnosis. Pernicious anæmia; hæmosiderosis of the liver and kidneys; marked hæmolysis in the hæmolymph glands; chronic catarrhal gastritis; fatty degeneration of the heart; megaloblastic red marrow.

CASE VI.—R. C. J., aged thirty-one years, American, army service, was admitted to the medical clinic April 19, 1901. Comes to the hospital for chronic diarrhœa and general weakness. Family history negative; previous history good. Present trouble began March, 1899, while with the United States army in the Philippines. Had what was called dysentery; eight to fifteen bloody stools a day; usually in the morning he would pass about a teacupful of slime and blood, with a little fecal matter. This attack lasted a month. Since that time he has had diarrhœa and vomiting; has no pain at stool. Has lost fifty-five pounds. Has irregular fever. At times he is so weak that he is obliged to go to bed. Fainted while going from waiting-room to ward.

Physical Examination. Greatly emaciated; musculature very small and soft. Panniculus very thin. Skin pale sallow, with yellowish tinge. No pigmentation. Nails and mucous membranes very pale. No œdema; no enlarged glands. Examination of the lungs negative. No apex-beat. Heart dulness not enlarged; sounds weak; no murmurs. Pulse regular, small, low tension. Liver and spleen not enlarged, not palpable. Marked succussion in the region of the umbilicus.

Blood Examination. Red cells, 1,200,000; leucocytes, 5700; hæmoglobin, 25 per cent.

Patient improved for a few days after entrance, but complained of night-sweats and sore mouth. No protozoa, worms, or eggs found in the stools. On May 13th he complained of great pain from hemorrhoids. Referred on May 19th to surgical clinic for operation. Blood examination before operation, May 20th: red cells, 850,000; leucocytes, 5602; hæmoglobin, 30 per cent.; specific gravity, 1040.

On June 1st a small fistula developed near the anus, and a hard swelling appeared near this somewhat later. The patient gradually became weaker and more emaciated; pulse small and weak. Mind became clouded. On July 6th he became unconscious at 9 A.M., remaining so until death, at 12.45 noon.

Clinical Diagnosis. Pernicious anæmia; chronic dysentery; ischiorectal abscess.

Autopsy by Dr. Warthin, 2 P.M., July 6, 1901.

Autopsy Protocol. Cadaver 157 cm. long. Frame small; much emaciated. Muscles small; on section, brown in color, tear easily. Rigor mortis present only in the muscles of the jaw. Panniculus almost absent; on section, orange-yellow. Skin very pale, with light lemon tint; no hemorrhages. Sclerotics slightly yellowish. Slight œdema at the ankles. Very slight hypostasis over the back. No pigmentation. Brain and spinal cord not examined (no permission).

Diaphragm, fifth rib on the right, fifth interspace on the left. Position of the thoracic organs normal. Mediastinal fat in small amount; no remains of the thymus. No fluid in the pleural cavity; no pleural adhesions.

Pericardial sac contains 20 c.c. of slightly cloudy, yellowish fluid. Pericardium normal. Heart weighs 256 grammes; rather small. Epicardium somewhat opaque; subepicardial fat small in amount, fat tissue semifluid. Heart muscle reddish-brown; tears easily. Left ventricular wall, 15 mm. thick; right, 2 to 5 mm. Chordæ tendineæ somewhat shortened. Endocardium of the left auricle thickened. Mitral orifice somewhat thickened; otherwise valves are negative. Foramen ovale is closed, but in the auricular septum there are several small, communicating openings covered by a thin membrane on the right side.

Both lungs voluminous; moderate anthracosis; upper lobes pale, lower ones dark red; on pressure yield abundant foamy exudate. In the right lower lobe a small mass of calcification. Pleura entirely free; slightly thickened over the upper right lobe. Pulmonary vessels, bronchi, and bronchial glands negative. Small patches of sclerosis in the aorta. Thoracic ducts negative. Upper respiratory tract negative except for paleness of mucosa. Thyroids moderately enlarged; parathyroids small, brown. Cervical hæmolymph glands enlarged, brownish-red in color.

About 90 c.c. of fluid in the peritoneal cavity. Peritoneum negative. Omentum poor in fat, rolled up; fat of a clear, hyaline appearance. Position of the abdominal organs normal.

Spleen weighs 96 grammes; small, triangular in shape. Small notch at the lower portion of the anterior margin. Capsule thickened and wrinkled. Small white, pearly nodules scattered over the surface. On section, stroma increased; follicles few, consistency soft, color brownish-red.

Adrenals negative, save for beginning post-mortem change.

Left kidney weighs 184 grammes; right, 176 grammes. Fatty capsule of both poor in fat. Fœtal lobulation of kidneys preserved to a slight extent. Color deep brownish-red. A number of small hyaline nodules, the size of a pin-head, found in the cortex of both kidneys; some of these have yellow centres. Ureters negative. Bladder greatly distended, filled with clear, yellow urine.

Stomach contains about 100 c.c. of greenish-yellow fluid containing milk curds and a large amount of mucus. Mucosa pale, thickened, especially toward the pylorus. In the fundus are two large ulcers in process of healing, and one completely healed. Mucosa covered with grayish mucus.

Intestines filled with soft, yellowish, unformed feces. Mucosa very pale; small, punctiform hemorrhages in the lower part of the small intestine. No ulcers. Colon filled with light yellow, unformed feces. Mucosa pale, containing small punctiform hemorrhages. No ulceration; no parasites.

Liver weighs 1136 grammes; small, rather round in shape, light chocolate color. Beneath the capsule a number of small cysts, the size of a pin-head to a small pea. Wall of cyst thick and hyaline. No pus, no parasites found in the cysts. On section, liver is anæmic, yellowish-brown; consistence firm, lobules fairly distinct. Gall-bladder, bile passages, and portal vein negative.

Pancreas firm, light brown in color. Near the head there is a small reddish body, the size of a pea. Several large Pacinian corpuscles near the pancreas.

Mesentery poor in fat. Glands greatly enlarged, not pigmented. On section, many are reddish or pink.

Retroperitoneal glands enlarged; the hæmolymph glands much enlarged and of a chocolate-brown color.

Genitals small, otherwise negative. Tissues about the rectum thickened and infiltrated. Rectal fistula opening through the perineum, near the anus, filled with gauze; purulent discharge. No tubercle bacilli in the pus.

Red marrow hyperplastic; no changes in the fatty marrow or the long bones of the lower extremities. Peripheral lymph glands not enlarged.

Microscopic. Heart. Brown atrophy and fatty degeneration.

Lungs. Atrophy, œdema, healed tubercles.

Spleen. Marked atrophy; no hæmosiderosis.

Kidneys. Atrophy; connective tissue increased; slight hæmosiderosis of convoluted tubules; small hyaline scars (tubercles?).

Stomach. Chronic gastritis, with hyperplasia; healing ulcers.

Intestines. Chronic enteritis.

Liver. Atrophy; hæmosiderosis of the peripheral zone of lobule; small degeneration cysts (?).

Pancreas. Fatty infiltration, slight hæmosiderosis.

Bone Marrow. Megaloblastic; no lymphoid areas in the fatty marrow.

Hæmolymph Glands. See below.

Pathological Diagnosis. Pernicious anæmia; chronic enteritis; healing gastric ulcer; rectal fistula; hæmosiderosis of the liver, kidneys, etc.; general atrophy; fatty degeneration of the heart.

Case VII.[1]—J. L., aged sixty-one years, German, farmer by occupation, was admitted to the medical clinic December 5, 1901. Patient came to the hospital because of "gas on the stomach," vomiting at times; heavy pain in the stomach after eating; loss of weight and strength. Family history negative. Had good health up to the age of fifty years, at that time had a severe attack of "dysentery," lasting several weeks. After this his stomach began to trouble him; pain and shortness of breath until relieved by eructations of gas. Starchy foods gave the most trouble. Had a sour vomitus which "bit" his mouth. This condition lasted until one year ago, when he began to lose his appetite and strength. At times when he is feeling worse his skin becomes quite yellow. His mind has been much disturbed; has had persecution delusions, and at one time attempted to murder his family. Has had lumbago and slight attacks of "rheumatism." Bowels regular for the greater part of the time, but has attacks of diarrhœa lasting several days.

Physical Examination. Patient looks very ill; markedly cachectic; expression weary and drawn; active dorsal position. Height five feet nine inches. Present weight, 114 pounds; ten years ago weighed 156 pounds, one year ago 130 pounds. Limps in walking; has a slight lateral curvature, causing prominence of the left side and scapula. Musculature small and flabby. Panniculus absent. Skin loose, inelastic, dry, extremely sallow, with yellow tint. Scleræ white. Mucous membranes rather pale. Tongue small, smooth, without coat; papillæ very short. Teeth rotten; only a few snags in the mouth.

[1] Cases VII. and VIII. have been added since the meeting of the Association.

Slight soreness of the gums. No œdema at the ankles. Examination of the joints negative. Jugulars very prominent.

Lung boundaries, sixth rib on the right, sixth intercostal space on the left. Hyperresonance all over. Auscultation negative.

Percussion of the heart negative. Low-pitched, rather harsh, systolic murmur at the apex, scarcely heard in the left axilla. Second sound at the apex not made out. Pulmonary second not accentuated; aortic second negative. Radial artery shows diffuse hardening. Pulse, 52 to 54; regular, moderately strong.

Edge of ribs touches the iliac crest. Thorax appears pressed in at the sides. Double inguinal hernia, most marked on the left. Abdomen below the level of the ribs, slightly fuller below the umbilicus. Pubes very prominent. Abdominal walls very thin and lax. Liver dulness extends to the margin of the ribs; liver not distinctly palpable. Splenic dulness not enlarged; organ not palpable. Distention of the stomach not satisfactory. Digital examination of the rectum showed internal piles; prostate not enlarged.

Blood Examination, November 9th. Red cells, 1,626,400; leucocytes, 4838; hæmoglobin, 40 per cent. Differential count of 242 cells: lymphocytes, 14.5 per cent.; mononuclears, 8 per cent.; polynuclears, 54 per cent.; eosinophiles, 1 per cent.; degenerating, 22 per cent.; megaloblasts, 0.5 per cent. Poikilocytosis very marked; many megalocytes—about 33.3 per cent.

Examination of the stomach washing after a test-meal showed a moderate amount of mucus, a small amount of pus, no free or combined HCl, no starch digestion, positive lactic acid test. Urine contained numerous cylindroids and a few hyaline casts.

Patient's condition remained about the same for some time. On February 27, 1902, he was referred to the surgical clinic for operation for piles. On March 10th the lower extremities became œdematous. The last blood examination, made on March 25th, showed marked improvement; both hæmoglobin and the number of red cells increased. After this time he began to fail rapidly. Cystitis followed the operation for hemorrhoids. Condition of the mind worse; attempts starvation. Discharged April 24th. After leaving the hospital grew worse rapidly. Complete loss of mental powers. Skin very yellow at times, with small, scattered hemorrhages over the trunk and abdomen. Died May 17, 1902.

Autopsy at patient's home by Dr. Warthin, May 18th.

Autopsy Protocol. Body of medium build; slight posterior and lateral curvatures; lower edge of ribs touches the iliac crest; left side very prominent; musculature very small; great emaciation. No panniculus. Lower extremities œdematous. Skin dark sallow, with decidedly yellow tinge; dry and rough. Numerous punctiform hemorrhages over the trunk and thighs. Pigmented patches over the face and arms. Teeth absent; gums ulcerated. Rigor mortis present throughout. Abdomen scaphoid; much below the level of the ribs. On section, the muscles are deep brown in color and very dry. Fat tissue deep orange yellow.

Heart small, very soft, and flabby. Few small punctiform hemorrhages in the pericardium. Large tendinous spots on the anterior and posterior surfaces. Subepicardial fat greatly increased; light orange-yellow, near the apex showing serous atrophy. Large ante-mortem

clots in the auricles. Heart muscle pale yellowish, very soft, and easily torn. Right ventricle dilated. Slight calcification and thickening of aortic flaps; large patch of calcification in the endocardium of left ventricle; otherwise the heart is negative.

Lungs very voluminous. No fluid in the cavities. Few small adhesions. On section, very pale; slight anthracosis; much œdema. Areas of bronchopneumonia in the right lower lobe. Bronchial glands negative. No fluid in the peritoneal cavity. Large intestine moderately distended; stomach and small intestines collapsed; stomach lying almost vertically, the pylorus below the level of the umbilicus. Spleen large, extending below the edge of the ribs. Liver about a hand's breadth above the edge of the ribs, in the right nipple line. Omentum poor in fat, of a deep orange-yellow.

Spleen about four times the normal size; capsule stretched, smooth. On section, deep red in color, very soft. Trabeculæ and follicles covered up by pulp.

Adrenals slightly atrophic; otherwise negative.

Both kidneys smaller than normal. Fatty capsules well developed; fibrous capsules adherent. Cortical surfaces rough and irregular. In both kidneys numerous soft, yellowish elevations scattered over the cortical surface. Around some of these there is a reddish zone. On section, both kidneys show abscesses of varying size, extending from the pelvis to the cortex, forming the yellowish elevations seen on the latter. Kidney substance between the abscesses is pale yellow, cloudy, and softened, containing numerous hemorrhagic areas. Pelves dilated; mucosa thickened and covered with purulent exudate. In the exudate are numerous small gritty particles. Both ureters dilated; the mucosa thickened. Bladder wall greatly thickened; in the mucosa are numerous ulcers of varying size, having undermined edges and filled with pus and phosphatic sand. Prostate small. Genitals negative.

Mucosa of the small intestine atrophic, very anæmic. Large intestine filled with soft, pale yellow feces. Mucosa very pale. Internal hemorrhoids. Slight double inguinal hernia, the folds of the small intestine resting loosely in capacious shallow sacs, without adhesions.

Stomach very small; contains about 250 c.c. of thick mucus, with food remains. The shape of the organ resembles that of a long-handled gourd, the atrophic pyloric end forming the handle, the body being formed by the fundus and cardiac end. The diameter of the pyloric half of the stomach is less than that of the duodenum. The pylorus is free; admits the thumb. Mucosa of pyloric portion atrophic; no appearance of new-growth. Wall of pyloric portion thicker than that of fundus. Mucosa of the entire stomach covered with thick, grayish mucus.

Pancreas small; lobules atrophic; slight fatty infiltration.

Liver smaller than normal; rather round; left lobe atrophic. Capsule slightly thickened over the lower edge. On section, presents a nutmeg appearance, the general color being a deep reddish-brown. Bile-ducts patent. Gall-bladder small, filled with dark brownish bile.

Mesenteric glands somewhat more prominent than normally. On section, present no unusual appearance. Cervical, axillary, mediastinal, inguinal, and cubital glands not enlarged, apparently normal. At the brim of the pelvis, and extending upward along the aorta and vena cava, are about twenty enlarged and dark-red glands resembling hæmolymph

glands. The largest forms a cord 5 cm. long and 0.5 cm. in diameter. On section, these contain blood sinuses filled with blood. The other lymph glands in this region are pale or brownish, small, and on section appear atrophic. There is no hypostasis or hemorrhage in the neighborhood of these red glands, and they are found side by side with the pale glands. Around the renal vessels several similar deep-red glands the size of a coffee-bean are found. In many of the prevertebral lymphatics a pale red fluid is present; the lymphatics are greatly dilated.

The fatty marrow of the long bone of the lower extremities is deep red throughout, being apparently replaced by the lymphoid marrow.

The brain and spinal cord were not examined. (No permission. Owing to circumstances, no weights or measurements could be taken.)

Microscopic. Heart. Atrophy and fatty degeneration.

Lungs. Acute and chronic congestion, œdema, areas of bronchopneumonia.

Spleen. Atrophy, acute and chronic congestion, hyaline vessels, increase of the reticulum of pulp, great decrease of lymphocytes in pulp; the majority of the cells in the pulp are large mononuclear cells of varying size and shape. Many of these contain pigment, very little of which gives the iron reaction. They also contain red blood cells in different stages of disintegration. Larger cells containing two to three nuclei are also numerous in the reticulum and sinuses. A few large giant cells resembling those of the bone marrow also found. Many of the larger mononuclear phagocytes are colored brown or yellowish; in others the pigment is granular. Small collections of granular pigment of a brown color are found throughout the pulp. Only a small portion gives the iron reaction.

Adrenals. Negative; post-mortem change.

Kidneys. Cloudy swelling, atrophy, acute ascending pyelonephritis. Very little hæmosiderosis of the convoluted tubules.

Bladder. Chronic purulent cystitis.

Stomach. Chronic atrophic gastritis.

Intestine. Simple atrophy.

Pancreas. Atrophy, slight increase of interstitial connective tissue, moderate sclerosis of vessels.

Liver. Marked chronic congestion (nutmeg liver), lobules atrophic, marked hæmosiderosis of the peripheral portion of the lobules. In the cells of the central portion both hæmatoidin and hæmosiderin are present; many endothelial cells containing the latter are found.

Bone Marrow. Areas of lymphoid marrow in fatty degeneration; contain few nucleated red cells and few giant cells.

Lymph Glands. Atrophic; follicles of many glands contain hyaline masses; eosinophiles not increased. In the sinuses of many glands numerous red cells are found; also phagocytes containing red cells.

Hæmolymph Nodes. See below.

Pathological Diagnosis. Pernicious anæmia; hæmosiderosis of the liver; chronic cystitis; ascending pylonephritis; chronic atrophic gastritis; general atrophy and passive congestion; fatty degeneration of the heart; lymphoid marrow; hyperplasia of the hæmolymph glands.

CASE VIII.—Miss Mary McK., aged twenty-seven years, American, was admitted to the medical clinic June 7, 1902, complaining of "general weakness." Family history negative. Healthy as a child. Had

measles and whooping-cough. Three years ago had "malarial fever" while in Michigan; was ill with fever for about three weeks; no chills; never well since this attack. During the fever had pronounced epistaxis; this would occur without apparent cause. Has always had a tendency to nosebleed. Periods established at the age of twelve or thirteen years; regular; no unusual flow; continued regular up to one year ago, when they stopped entirely. Present trouble began three years ago. Became easily fatigued; at the same time she noticed that she was becoming pale. Appetite variable; sometimes has sharp pain in the stomach after eating; frequent nausea and vomiting. Vomitus always yellow, from bile; never dark. Is troubled with shortness of breath. Feet swell when she walks; last summer they were swollen all the time, the swelling extending as far as the knees. Often feels dizzy when walking. Has usually two to three loose stools daily. Since last spring has had hemorrhoids, which bleed occasionally but not profusely. Has frequent attacks of nosebleed, without apparent cause. Complains of blurring and "specks" before the eyes. Is better in winter.

Physical Examination. Patient looks very sick. Extremely pale and sallow. Very weak. Mind clear, but answers questions slowly. Voice weak. Mucous membranes very pale. Scleræ white, with a yellowish layer of fat beneath the conjunctiva. Teeth fairly good; several extracted. Height, five feet six inches; weight, 105 pounds (best weight, 140 pounds).

Auscultation and percussion of the lungs negative. Broad area of pulsation over the præcordium. Pulsation very rapid. Apex-beat best felt in the fourth intercostal space, in the nipple line. Distinct pulsation in the third intercostal space, in the nipple line, extending to the nipple. Distinct systolic thrill over the greater part of the præcordium. Dulness begins on the third rib, extends to within 1 cm. of the nipple, and extends a slight distance to the right of the sternum, in the fourth intercostal space. Loud, rather harsh, systolic murmur at apex, followed by a soft, distinct diastolic murmur, best heard inside and above the nipple, and well transmitted to the left axilla. In the fifth intercostal space, to the left of the sternum, there are loud, blowing systolic and diastolic murmurs; same in the left second interspace, much weaker in the right second interspace, but very loud in the middle of the sternum, opposite the third costal interspace. Pulse, 124; small, low tension; artery not thickened.

Abdomen, slightly below the level of the ribs, shows a prominence of the shape of the stomach just below the navel. Succussion sounds in this region. Right kidney distinctly palpable; left not satisfactorily felt. Liver dulness very broad, extending from the fifth rib to the margin of the ribs. Thin edge of the liver can be felt. Splenic dulness greatly enlarged, extending from the seventh intercostal space to the margin of the ribs and forward into Traube's space, combining with heart dulness to make this space completely dull. Spleen not satisfactorily felt.

Blood Examination. Red blood cells, 704,000; leucocytes, 2037; hæmoglobin, 13 to 15 per cent. (June 11, 1902). On the 20th the red cells were 546,000; hæmoglobin, 14 per cent. Poikilocytosis and endoglobular degeneration marked. Numerous normoblasts and megaloblasts.

Urine contained traces of albumin; no casts.

Patient rapidly grew worse, irregular fever, reaching 102° F. at times; vomiting, hemorrhage from the bowels, etc. Died June 25th, at 6.20 A.M.

Autopsy by Dr. Warthin at 7 P.M. of the same day.

Autopsy Protocol. Body slender; 157 cm. long. Thorax long and narrow below; the right side anteriorly more prominent than the left. Abdomen above the level of the ribs, the distention greatest just below the umbilicus. Musculature small; much emaciated. On section, muscles are pale and moist; do not tear easily. Fair amount of panniculus. On section, light golden-yellow, slightly moist. Trace of œdema over the ankles. Rigor mortis is present throughout. Trunk is slightly warm. Skin is very pale sallow, with slight yellowish tint. Very pale hypostasis over back. A number of bluish areas (angiectatic veins) about both ankles. Numerous small, pigmented lymphangiomata over the radial side of both forearms. No punctate hemorrhages found anywhere in the skin. Mucous membranes very pale. Teeth in good condition; upper molars absent. Slight layer of yellowish fat over sclerotics.

Brain and spinal cord not examined. (No permission.)

Diaphragm at the level of the fourth interspace, on both right and left. Mammæ negative. Apex in the left nipple line, fourth interspace. Heart extends a slight distance beyond the right sternal line. Mediastinal fat in fair amount; light yellow color. No remains of thymus. Pericardial sac lax; contains about 30 c.c. of clear fluid. Heart weighs 332 grammes; larger than cadaver's right fist. Both ventricles dilated. Small tendinous spot on the anterior wall of the right ventricle; otherwise pericardial surfaces are normal. Subepicardial fat greatly increased, completely covering the right ventricle with a thick layer. No hemorrhages beneath the pericardium. Heart contains pale, watery blood, and a very thin layer of whitish clot covers the endocardium of the right ventricle and auricle. Wall of the left ventricle measures 8 to 12 mm. Ventricular cavity greatly dilated, the muscle trabeculæ flattened. Heart muscle is a very pale yellowish-brown; cloudy, cooked appearance; is very soft and easily crushed. The columnæ carneæ show a moderate degree of "tiger heart." Right ventricle is greatly dilated; wall measures 6 to 8 mm., 3 to 5 mm. being of fat. The mitral orifice admits three fingers; valves normal. Aortic admits the thumb; semilunar valves negative. Tricuspid greatly dilated; admits the entire hand; flaps negative. Pulmonary orifice and valves negative.

Slight amount of clear fluid in both pleural cavities. Left lung weighs 54.5 grammes. Pleura entirely free; clear, moist, shining. Lung moderately voluminous; upper lobe very pale, moderate hypostasis in the lower. On section, the parenchyma yields an abundant fluid exudate on slight pressure. Slight anthracosis. No airless areas. Two small, pigmented healed tubercles beneath the pleura. Right lung weighs 52.8 grammes. Few old adhesions in the pleura. On section, similar to the left lung. Pulmonary vessels negative. The bronchi are filled with foamy fluid; mucosa very pale. Bronchial glands moderately anthracosed. Œsophagus and thoracic vessels negative. Cervical glands negative. Mouth and throat not examined. Thyroid small.

No fluid in the peritoneal cavity. Peritoneum moist, negative. Omentum rich in fat of a light yellow color. No subperitoneal hemorrhages. A number of small, pale-pink lymph glands in the omentum, near the greater curvature of the stomach. Position of the abdominal organs negative.

Spleen weighs 336 grammes and measures 15 x 9.5 x 4 cm.; enlarged. Capsule stretched; shows a number of patches of hyaline thickening over the anterior surface. No notches in either the anterior or posterior edges. Shallow furrow on the anterior surface, near the upper fourth. Consistency very firm; does not flatten. On section, very anæmic; pulp bluish-red, swollen, and granular, covering up the follicles. Pale-pink infarct near the upper pole, extending into the organ in wedge-shape. Consistency of infarct firmer than that of surrounding pulp.

Adrenals negative. Slight post-mortem change in medullary portions. Left kidney weighs 19.2 grammes; normal in size and shape. Right kidney weighs 17.6 grammes. Both kidneys present the same appearance. Fatty capsules very rich in pale yellow fat; fibrous capsules strip easily. Venæ stellatæ not shown. Consistency of kidneys very firm. Color, pale pinkish brown. Very anæmic; outlines of kidney structures not well marked. Surface very glistening, semitranslucent, suggesting amyloid change. Ureters and bladder negative.

Stomach rather large, dilated; contains about 200 c.c. of sour-smelling food-remains. Wall very thin. Mucosa white, smooth, and thin. Advanced post-mortem digestion. Duodenum contains yellowish fluid, with food-remains; sour odor. Mucosa very pale; thickened between the atrophic folds; appearance resembles the "état mammelonné." Ileum distended; contains very pale, soft fecal material. Mucosa atrophic; very pale. No enlargement of Peyer's patches or solitary follicles; no hemorrhages; no parasites. Appendix 10 cm. long, very slender; narrow lumen, containing light-colored fecal material; has large mesentery. Cæcum distended. Colon distended above the sigmoid, containing gas and soft, light-colored feces. No blood; no evidences of hemorrhage. Mucosa pale brown. Sigmoid contracted, empty. Upper portion of the rectum contains pale, putty-like feces. No signs of blood. Mucosa of the lower portion of the rectum injected. Just above the anus there is a ring of flattened hemorrhoids completely encircling the bowel. From these there is evidence of hemorrhage in the shape of fresh blood and small clots. On section, the tissue of the submucosa about the hemorrhoids is infiltrated with blood. Hemorrhage is apparently by diapedesis. Mucosa of the anus is contracted; covered with a whitish coating, as if from the action of some caustic.

Liver is enlarged, weighing 2624 grammes. Breadth, 27 cm. Right lobe measures 23 x 19 x 5 cm.; left lobe, 11 x 8 x 4 cm. Rather flattened; the sagittal diameters increased. Slight thickening of the capsule along the lower edge (slight corset liver). Anomalous furrow in the upper part of the left lobe. On section, very anæmic; central veins show only in the peripheral portions of the organ; here they are much dilated, giving a marked nutmeg appearance. Cut surface is pale yellowish-brown, the central zones of the majority of the lobules being a lighter yellow; peripheral portion browner. Slight fatty smear. Surface shows fatty shine. Gall-bladder is very small, not dilated,

Contains very thick brownish bile, with a small amount of coarse dark sand, composed of pigment; largest, the size of a mustard-seed. Bile passages patent. Pancreas very pale; shows beginning post-mortem changes. Portal vein negative.

External genitals negative. Uterus, 3.5 cm. long; breadth of fundus, 3 cm.; of cervix, 1.5 cm. Endometrium negative. Vagina very small; rugæ marked. Hymen apparently intact. Ovaries of normal size; ripe follicle on the surface of the left.

Peripheral lymph glands small and pale. Mesenteric glands not enlarged; very pale. No enlargement of the prevertebral glands; the lymph glands small and very pale; the hæmolymph glands not hyperplastic, and distinguished from the former only by their uniform pale pink color. Small amount of pale red fluid in the lymphatics.

Body contains very little blood.

Fatty marrow of the long bones completely converted into deep-red lymphoid marrow.

Microscopic. Lungs. Atrophy, acute congestion, and œdema.

Heart. Fatty degeneration, infiltration, and cloudy swelling.

Spleen. Marked congestion, atrophy of the lymphoid tissue of pulp, hyperplasia of the reticulum; blood spaces in many places appear gland like, lined by hypertrophic endothelium. Many cells along the walls of the sinuses show phagocytic action, containing red cells in various stages of disintegration, and a diffuse yellow pigment which does not give the iron reaction. No trace of iron reaction in the spleen. Follicles very atrophic, widely separated.

Adrenals. Negative.

Kidneys. Simple atrophy, great increase of interstitial connective tissue. Cells of convoluted tubules filled with coarse granules of yellowish-brown pigment, giving the iron reaction. Greater amount of hæmosiderin in the kidney than in the liver. Small nodules of calcification in the connective tissue. No amyloid.

Liver. Lobules atrophic. Marked fatty degeneration of the liver cells in the central portion of the lobules. Very little pigment in the degenerated cells, the hæmosiderin in the central portion of the lobules being almost entirely in the endothelial cells. Moderate hæmosiderosis of the liver cells of the peripheral portion. In some areas the capillaries of the central zone are greatly dilated. A few small collections of leucocytes in Glisson's capsule.

Stomach. Atrophic; shows complete post-mortem necrosis of the mucosa.

Duodenum. Chronic hyperplastic duodenitis.

Pancreas. Post-mortem change.

Lymph Glands. Atrophic; large masses of hyalin in the follicles of many of the glands. Bloodvessels dilated. Lymph sinuses dilated, containing many red blood cells; also phagocytes containing disintegrating red cells.

Hæmolymph Glands. See below.

Bone Marrow. Fatty marrow completely replaced by lymphoid marrow containing few nucleated red cells and few giant cells.

Pathological Diagnosis. Pernicious anæmia; hæmosiderosis of the liver and kidneys; fatty degeneration and dilatation of the heart; chronic duodenitis; general atrophy; lymphoid transformation of fatty marrow.

LYMPH GLANDS.—Gross Appearance.

Case.	Peripheral.	Mesenteric.	Prevertebral.	Hæmolymph.
1	Slightly enlarged; more or less brown pigmented.	Slightly enlarged; pale pink.	Enlarged; brownish-red.	Enlarged; brownish-red.
2	Not enlarged; negative.	Not enlarged; negative.	Not enlarged; pinkish or brownish.	Not increased in number; not enlarged; pink or brownish; three in omentum pink.
3	Not enlarged; negative.	Not enlarged; negative.	Greatly enlarged; red.	Enormously enlarged (lymphosarcoma?) red.
4	Negative.	Moderately enlarged; pale, homogeneous.	Greatly enlarged; brown color.	Enlarged; brownish.
5	Not enlarged; negative.	Not enlarged; negative.	Majority appear to be hæmolymph glands, red or bluish-red; largest size of bean.	Apparently greatly increased in number; red to blue-red; not enlarged; size of mustard-seed to pea.
6	Not enlarged; negative.	Enlarged; reddish or pink; not pigmented.	Enlarged; brownish.	Enlarged; chocolate-brown.
7	Not enlarged; normal.	Prominent; otherwise negative.	Atrophic; pale or brownish.	Enlarged; deep-red color; sinuses greatly distended with blood.
8	Small and pale.	Not enlarged; very pale.	Small and pale.	Not enlarged; pale pink; sinuses distended with pale blood.

Microscopical.

Case.	Peripheral.	Mesenteric.	Prevertebral.	Hæmolymph.
1	Deposit of hæmosiderin.	Congested; in many red cells and pigmented phagocytes in the lymph sinuses.	Moderate hyperplasia; hæmosiderin deposit; many congested, contain red blood cells in lymph sinuses.	Hyperplastic; sinuses dilated; increased hæmolysis; hæmosiderosis.
2	Negative.	Negative.	No hyperplasia; hæmosiderin deposit in some.	No hyperplasia, only slight increase of hæmolysis.
3	Negative.	Negative.	Extreme hyperplasia resembling sarcoma, but containing lymph sinuses filled with red blood cells.	Tumor masses of the nature of hyperplastic hæmolymph glands or hæmolymphosarcoma; marked hæmolysis; little hæmosiderin; increase of eosinophiles.
4	Negative.	Negative.	The sinuses of the majority contain phagocytes filled with pigment.	Sinuses filled with phagocytes containing red cells and pigment; increase of eosinophiles.
5	Negative.	Negative.	Apparently all hæmolymph glands; sinuses filled with blood and phagocytes.	Sinuses filled with phagocytes containing red cells and pigment; increase of eosinophiles.
6	Negative.	Lymph sinuses contain many phagocytes, disintegrating red cells, and pigment.	Majority apparently hæmolymph glands; sinuses filled with blood and phagocytes.	Sinuses filled with pigment containing phagocytes; much hæmosiderin; increase of eosinophiles.
7	Negative.	Negative.	Atrophic; hyaline masses in follicles; red cells and phagocytes in sinuses.	Atrophy of lymphoid tissue; sinuses dilated; many phagocytes; small amount of pigment.
8	Negative.	Negative.	Atrophic; lymph sinuses dilated contain red-cells and phagocytes.	Atrophic; increased hæmolysis; many phagocytes containing red cells, but little pigment; hyaline deposit; sinuses dilated.

General Summary of Cases. *Clinical.* The clinical features presented by these eight cases are very similar—progressive weakness and paleness, shortness of breath, gastric disturbances, diarrhœa, slight irregular fever, tendency to hemorrhages, low red blood cell count, relatively high hæmoglobin, presence of nucleated red cells, low leucocyte count, etc.

Pathological. In all eight cases no direct cause for the anæmia was found. The general pathological findings were the same—hæmosiderosis of the liver and kidneys, fatty degeneration and infiltration of the heart, general atrophy, passive congestion and œdema, punctiform hemorrhages, etc. In two cases no changes in the stomach were found, in four chronic atrophic gastritis was present, in one case chronic hyperplastic gastritis, and in one case simple atrophy of this organ. In three cases the fatty marrow showed no lymphoid transformation, in two cases small points of lymphoid change occurred throughout the fatty marrow, while in three cases the fatty marrow of the long bones was completely changed into lymphoid marrow.

The diagnosis of pernicious anæmia may be safely based upon the above characteristics in all of the cases with the possible exception of No. 3. Both the clinical symptoms and the pathological findings make this case unique. The marked tendency to hemorrhage, the active hæmolysis in the circulating blood as shown by the blood examinations, the sarcoma-like hyperplasia of the retroperitoneal lymph glands, make the diagnosis doubtful, and both Dr. Dock and myself have hesitated in classifying this case under any definite head. Since the hyperplastic changes in the retroperitoneal lymph glands appear to take their origin from the hæmolymph glands, I have included this case in this group, although the diagnosis of the early stage of leukæmia, lymphosarcoma, or hæmolytic poison must also be considered.

It will be seen from the above that the changes in both lymph and hæmolymph nodes vary greatly in degree. In one case only did the peripheral glands (axillary, superficial cervical, inguinal, and cubital) show any change that could be regarded as belonging essentially to pernicious anæmia. Likewise the changes in the mesenteric glands were not constant, occurring in but two cases. But in all eight cases changes were found in the prevertebral, retroperitoneal, and cervical lymph and hæmolymph glands, indicating a degree of hæmolysis greater than that found, either under normal conditions or in such diseases as chronic tuberculosis, typhoid fever, sepsis, etc., in which evidences of increased destruction of red cells are also found in these glands. These changes may be summed up as follows: Apparent increase in the number or hyperplasia of resting hæmolymph glands, dilatation of the blood sinuses, with increase of phagocytes containing disintegrating red cells and pigment; in the lymph glands, dilatation of

the lymph sinuses, presence of an inceased number of red cells in the latter, increased number of phagocytes, and congestion.

These changes differ so greatly in degree in the different cases as to suggest intermittent rather than continuous hæmolysis. In Case II. the evidences of hæmolysis were not much greater than normal; in Cases VII. and VIII. there was great increase in the number of phagocytes containing red cells, but little pigment; in Cases III., IV., V., and VI. the sinuses were filled with pigment-containing phagocytes giving but little iron reaction; while in Case I. the glands were filled with granular hæmosiderin, both free and in phagocytes. It seems reasonable to explain these various findings by the theory of intermittent or cyclical hæmolysis, death in the different cases occurring at different stages of blood destruction. This theory is borne out by the clinical history of exacerbations in the symptoms of anæmia, intoxication, etc. In three cases (I., V., and VI.) showing a more malignant and rapid termination, the patient dying during an exacerbation, the evidences of hæmolysis in the glands were more marked; in the cases dying of progressive weakness, cardiac dilatation, etc., without especial exacerbation, the findings are those of less active hæmolysis (Cases II., VII., VIII.).

There is also good reason to believe that in some cases the spleen is the most active seat of hæmolysis; in others the hæmolymph glands. This is based upon the fact that in some cases very little hæmosiderin or few phagocytes containing red cells are found in the spleen, while they are abundant in the hæmolymph glands. In other cases pigmented phagocytes are more numerous in the spleen. Either the poison causing pernicious anæmia acts differently at different times upon the hæmolytic organs, or more than one hæmolytic poison may lead to the disease by stimulation of either splenic, lymphatic, hæmolymphatic, or bone-marrow hæmolysis. In some cases splenic hæmolysis may predominate, in others hæmolymphatic. It may be possible that varieties of pernicious anæmia (splenic, hæmolymphatic, etc.) may be distinguished. At present nothing can be regarded as proved with respect to these points, inasmuch as we know nothing at all concerning the nature of the hæmolytic poison of this disease.

The human hæmolymph glands may be divided into three groups with reference to the relationship between the lymph and blood systems:

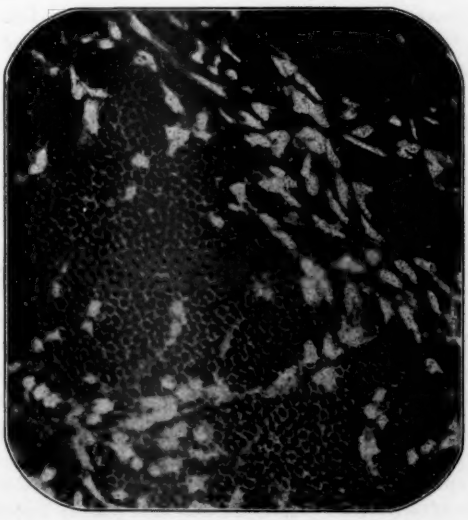
1. Glands with blood sinuses only.
2. Glands with blood sinuses communicating directly with lymph sinuses.
3. Glands with very slight capillary connection between bloodvessels and lymph sinuses.

The second and third varieties are of most common occurrence in man; the first variety in the sheep, goat, and ox. Under normal conditions

FIG. 1.

Hæmolymph gland, showing dilated blood sinuses; dark areas = blood in sinuses; light areas = lymphoid tissue. × 150.

FIG. 2.



Higher power view of blood sinus from same gland as in Fig. 1, showing the sinus filled with red blood cells, and the delicate reticulum traversing the sinuses. × 750.

the amount of blood passing directly into the lymph is probably very small, and the majority of red cells are destroyed by the phagocytes in the lymph sinuses. A certain number of red cells escape these, so that the lymph from these glands always contains a certain number of red cells, this having been interpreted by some observers as proof of the formation of red cells by lymph glands. The majority of mesenteric and retroperitoneal glands probably belong to the third class.

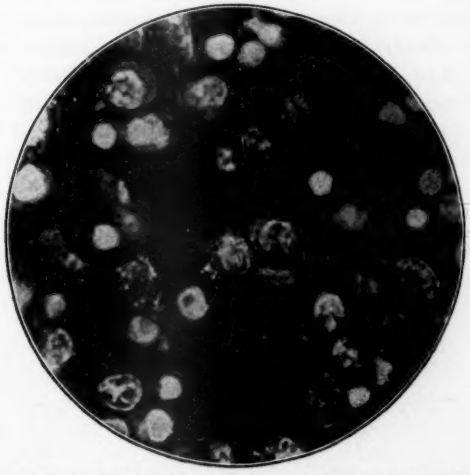
There is, therefore, always a certain amount of normal hæmolysis taking place in these glands. Under pathological conditions of congestion and inflammation the number of red cells passing into the lymph sinuses to be destroyed—in part, at least, by the phagocytes—is greatly increased, to such an extent sometimes that the lymph sinuses become filled with blood, and the glands come to resemble the hæmolymph glands of the first variety. The increased influx of blood into the sinuses leads always to an increased formation of phagocytes, these rising apparently from the endothelial cells lining the sinuses. The abnormal degree of hæmolysis thus produced occurs in the majority of infective processes, particularly in sepsis, typhoid fever, and chronic tuberculosis, and may be produced by certain poisons which cause congestion of the lymph glands. Further, lymphatic glands which are not hæmolymph glands may become so congested that diapedesis of red cells into the lymph sinuses occurs, the same phenomena of phagocytosis and hæmolysis taking place. This is particularly well seen in the regional lymphatics in the case of local infections. In infective diseases the specific poison when absorbed into the general circulation may stimulate the phagocytes of the spleen and hæmolymph glands to increased hæmolytic activity either directly or through injury of the red cells. The hæmolymphatic hæmolysis of pernicious anæmia is not specific in kind, and it is probable that other infections or intoxications may produce as severe a degree.

The hæmolysis of pernicious anæmia does not differ in kind from that occurring normally or in certain diseased conditions; the difference is one of degree only.

It is not the object of this paper to overemphasize the actual amount of hæmolysis occurring in the lymphatic and hæmolymphatic glands in pernicious anæmia; the main object is to call attention to the fact that hæmolysis may occur in this disease to a greatly increased degree in these structures as well as in the spleen. The conclusion to be gathered is that the hæmolytic poison does not confine its effects to the portal areas as claimed by Hunter, but is present in the general circulation. Further, as has been pointed out by Hunter, the hæmolysis of pernicious anæmia is a *cellular* process, and is performed by the phagocytes of the spleen, lymph glands, hæmolymph glands, and bone marrow, in response to the direct stimulus of the poison or of blood cells injured by the poison.

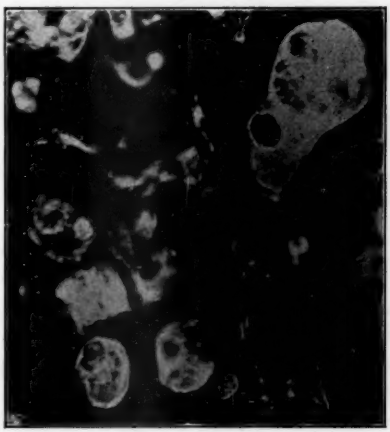
No evidences of the actual destruction of red cells are found in any organ or tissue except the spleen, lymphatic, and hæmolymphatic glands,

FIG. 3.



Large mononuclear cells containing hæmosiderin lying in meshes of the reticulum of the blood sinus. × 1000.

FIG. 4.



Phagocytes containing hæmosiderin from blood sinus of hæmolymph gland. × 1500.

and bone marrow. The hæmosiderin found in the liver and kidneys must exist in the circulating blood in the form of some soluble derivative of hæmoglobin which is set free at the seats of hæmolysis. This

is taken from the blood by the endothelial cells of the liver and kidney (rarely by those of other organs—pancreas, thyroid, adrenals, lymph glands, etc.) and transferred to the epithelial cells of these organs, thence to be excreted through the bile and urine. The occurrence of hæmosiderosis of the liver and kidneys in pernicious anæmia is therefore a secondary process only, and is characteristic of pernicious anæmia only in so far as the degree of hæmosiderosis is concerned. That the hæmosiderin is taken from the blood by the endothelial cells is well shown in Case VIII., in which in the majority of liver lobules the liver cells of the central portion of the lobules having disappeared,

FIG. 5.

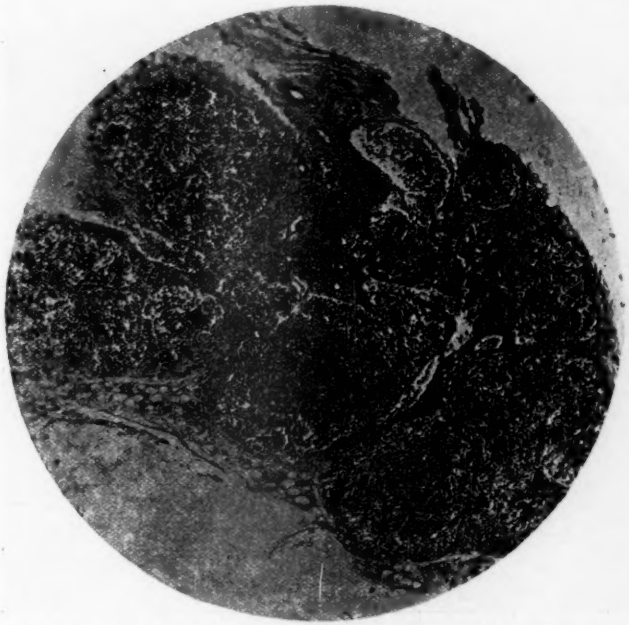
Section of tumor-like hyperplasia of retroperitoneal prevertebral glands in Case III. (angiectatic lymphosarcoma or hæmolymphosarcoma?). × 100.

as a result of chronic passive congestion, the pigment is found in the endothelium. Further, in animal experiments with toluylenediamine the hæmosiderin appeared first in the endothelium of the liver capillaries, and later in the liver cells.

In some of the cases there was an apparent increase of hæmolymph glands. At present it cannot be stated whether this is due to an actual new formation or to a hyperplasia of minute resting glands. It is more probable that the latter explanation is the correct one, the glands becoming more prominent as a result of their increased functional activity. The change in the lymphatic and hæmolymphatic glands to be regarded as many times, if not always, an important feature of the

pathology of pernicious anæmia, is *increase in the number of lymph glands showing diffuse red color, or spotting, or streaking with red.* That the changes described above occur in every case of pernicious anæmia cannot be proved by their occurrence in every one of my eight cases. The fact that such changes have been described so rarely might be explained by the rarity of changes in the peripheral and mesenteric glands, the likelihood of the retroperitoneal glands being left unexamined, the relatively insignificant character of the gross appearance,

FIG. 6.



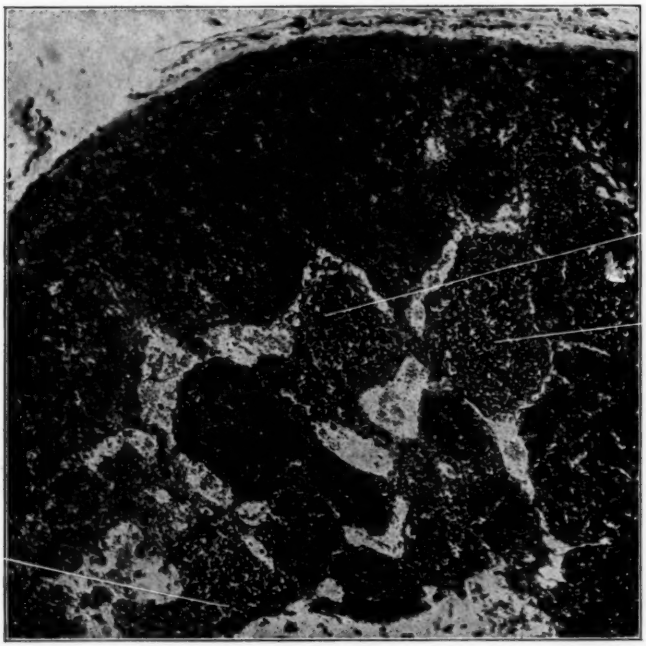
Cervical hæmolymph node from Case V. Peripheral sinuses filled with pigmented phagocytes. × 100.

and the fact that microscopic examination is necessary for the ultimate determination of the nature of the glandular changes. Increased hæmolysis may exist even in atrophic glands; hyperplasia is not an essential feature. The exact nature of the changes in the hæmolymph glands can be ascertained only by microscopic examination.

Weigert's case; the three cases, noted by Osler, of deep-red glands resembling spleen tissue; Schumann's case of enlarged and hemorrhagic glands; Müller's case of bright-red glands; the three cases of Eichhorst, I regard as resembling my cases, the red glands to be

hæmolymph glands or lymphatic glands showing increased hæmolysis. Three of my cases (V., VI., and VII.) were almost exactly like Weigert's case in the number of blood-containing glands and the large amount of blood in the lymphatics. *No evidence of red blood cell formation in the lymphatic or hæmolymphatic glands was seen in any of my cases. The presence of nucleated red cells in the sinuses is explained by their presence in the circulating blood.*

FIG. 7.



Retroperitoneal hæmolymph node from Case VII., showing great dilatation of blood sinuses. The dark areas are the blood sinuses filled with red cells and phagocytes; the light spaces are the dilated lymph sinuses containing lymph, but no blood. Example of gland with blood and lymph sinuses entirely separate. *a*, *a*, *a*. Small islands of lymphoid tissue. × 100.

Returning again to Case III., the great hyperplasia of lymphoid tissue containing blood sinuses apparently arising from the hæmolymph glands gives this case great pathological interest. The microscopic appearances suggest a direct conversion of fat tissue into lymphoid, and one is reminded of the new formation of hæmolymph glands occurring after splenectomy, as described by Tizzoni, Winogradow, Mosler, and myself. The term "hemorrhagic telangiectatic lymphoma," as applied by Mosler to such new formations, could be used in this

instance with propriety. The designation of "hæmolymphosarcoma" or "hæmolymphoma" also appropriately applies to the histological findings. An increase of eosinophiles in the hæmolymph glands was noted in four of my cases—in three associated with the presence of much pigment, in one case with little pigment.

Experimental. Hunter having shown that toluylenediamine caused hæmolytic action of the spleen similar to that of pernicious anæmia, experiments were undertaken to show the effects of this poison upon the hæmolymph and lymphatic glands. The sheep was chosen for the purpose, inasmuch as the hæmolymph glands in this animal are very large and numerous. In two cases—one of acute and the other of chronic poisoning with toluylenediamine—the hemolymph glands showed increased hæmolysis, as shown by the increased number of pigment and cell-containing phagocytes. Extreme congestion of the lymphatic glands was also produced, leading to diapedesis of red cells and hæmolysis in the lymph sinuses. Increase of eosinophiles was also noted in some of the glands. In a third sheep, splenectomized two months previously, intense hæmolysis was shown by these glands, and hæmosiderosis of the liver resembling that in pernicious anæmia. The increased hæmolysis in this case may be explained by the compensation on the part of the hæmolymph glands for the spleen. By these experiments it may be taken as proved that toluylenediamine excites not only the cell of the spleen to phagocytic hæmolysis, but also those of the lymph and hæmolymph glands. The close similarity between the action of toluylenediamine and the poison of pernicious anæmia is thus further shown.

Conclusions. 1. Pernicious anæmia is essentially a hæmolytic disease, the hæmolysis being due to some as yet unknown poison comparable in its effects upon the blood and blood organs to the action of toluylenediamine—whether auto-intoxication or infection, remains yet to be determined.

2. The poison of pernicious anæmia stimulates the phagocytes of the spleen, lymph and hæmolymph glands, and bone marrow to increased hæmolysis (cellular hæmolysis). Either the phagocytes are directly stimulated to increased destruction of red cells, or the latter are so changed by the poison that they themselves stimulate the phagocytes. The hæmolysis of pernicious anæmia differs only in degree, not in kind, from normal hæmolysis or the pathological increase occurring in sepsis, typhoid, etc.

3. It is not improbable that from the destruction of hæmoglobin poisonous products (histon?) may be formed which have also a hæmolytic action—a vicious circle of hæmolysis may thus be produced. No proof of this exists at present.

4. The hæmolysis of pernicious anæmia is not confined to the portal

area, as according to Hunter, but in some cases at least takes place also to a large extent in the prevertebral lymph and hæmolymph nodes and bone marrow. In the majority of cases the spleen is the chief seat of the blood destruction. No evidences of hæmolysis in the liver, stomach, and intestinal capillaries were found in the eight cases. The hæmosiderin of the liver and kidneys is carried to these organs as some soluble derivative of hæmoglobin, is removed from the circulation as hæmosiderin by the endothelium, and then transferred to the liver or kidney cells. The deposit of iron in these organs is of the nature of an excretion.

5. In the majority of cases only slight reaction for iron is found at the sites of actual hæmolysis (spleen, lymph, and hæmolymph glands and bone marrow). The greater part of the pigment in the phagocytes of the spleen, lymph, and hæmolymph glands does not give an iron reaction while in a diffuse form. When changed to a granular pigment the iron reaction may usually be obtained. The change to hæmosiderin is for the greater part accomplished by the endothelium of the liver and kidneys.

6. The varying pathological conditions found in these different cases of pernicious anæmia can be explained only by a theory of cyclical or intermittent process of hæmolysis. This theory is also borne out by the exacerbations so frequently seen clinically. The autopsy findings, in so far as evidences of hæmolysis are concerned, will depend upon the relation between the time of death and the stage of the hæmolysis.

7. The changes in the hæmolymph glands found constantly in these eight cases were: dilatation of the blood sinuses and evidences of increased hæmolysis, as shown by the increased number of phagocytes containing disintegrating red cells and blood pigment. In some of the cases these changes were accompanied by great increase in size and apparent increase in number of the hæmolymph glands; in other cases there was no hyperplasia, the only evidence of the changes present being that obtained by the microscopic examination. The changes found cannot be regarded as specific of pernicious anæmia, since it is probable that they may be produced by other infections or toxic processes characterized by great hæmolysis.

8. The lymphoid and megaloblastic changes in the bone marrow do not form an essential part of the pathology of pernicious anæmia, and are to be regarded as of a compensatory nature—an increased activity of red cell formation to supply the deficiency caused by the excessive hæmolysis.

NOTE.—The full bibliography of the references in this paper is omitted, because of its great length. My thanks are due to Dr. Bond, of Richmond, Ind., for the photographs for Figs. 1, 2, 3, and 4.

REVIEWS.

A TREATISE ON SURGERY BY AMERICAN AUTHORS, FOR STUDENTS AND PRACTITIONERS OF SURGERY AND MEDICINE. Edited by ROSWELL PARK, M.D., Professor of Surgery in the University of Buffalo, N. Y., etc. Third edition, in one royal octavo volume of 1350 pages, with 692 engravings and 64 full-page plates in colors and monochrome. New York and Philadelphia: Lea Brothers & Co.

THIS present edition, the third within five years, is much altered in appearance and also in the matter it contains. The form has been changed to one volume instead of two, and so much new material has been added that it appears more in the garb of a new work than as a new edition of an old and well-liked friend; and yet it has all the charm of clearness and the sequence in which the subjects are presented of the older volumes.

The publishers are to be congratulated upon the excellence of the paper, the clearness of the type, and the fineness of the illustrations, particularly the reproductions of the photomicrographs, which are exceptionally good.

The book is divided into six parts, with fifty-six chapters. Part I. deals with surgical pathology, and five of its six chapters have been written by the editor, who is peculiarly well fitted to present the latest and best theories on the subject. The pathology and examination of the blood as applied to surgery could scarcely be improved upon. Again, in Part II., which treats of surgical diseases, Park has written all the chapters but two, a guarantee of their clinical excellence and practical value. Part III. takes up the consideration of surgical principles and methods and minor procedures, including local and general anæsthesia. All of Part IV. is written by Nancrede, and treats of injury and repair. The chapter on gunshot wounds is particularly pleasing. In Part V. surgical affections of the tissues and tissue systems are considered. Perhaps the most interesting chapter here is on tumors, for Park presents the parasitic origin of malignant growths in a scientific and yet cautious manner, not forgetting to give the theories of Cohnheim their proper place and consideration. Knowing his decided views on this matter, we cannot but commend the modest way in which they are expressed, and the manner in which they are advanced. The chapter on the lymphatic system contains many new and excellent diagrams. The last part, on special and regional surgery, consists of more than half the pages of the book, and each article is written by a master of the subject. To pick out one chapter as more worthy of praise than another would simply mean that the subject chosen was more interesting to the reviewer than some other branches of surgery. For the same reason a just criticism could only be made in very minor

details, and this would scarcely be profitable when we consider how few surgeons are of one mind in minor details.

The book has been written for students, practitioners of medicine, and surgeons, and it accomplishes its purposes in a very commendable manner, for it is surely the most notable of all the single-volume surgeries. To the student it will prove of inestimable value on account of its clearness, conciseness, and logical sequence; to the practitioner of medicine it will be of great service, and for the accomplished surgeon it will have great interest and pleasure, for it will give him much food for careful thought.

R. G. Le C.

THE ARTIFICIAL FEEDING OF INFANTS. Including a Critical Review of the Recent Literature of the Subject. By CHARLES F. JUDSON, M.D., Physician to the Medical Dispensary of the Children's Hospital; and J. CLAXTON GITTINGS, M.D., Assistant Physician to the Medical Dispensary of the Children's Hospital. Pp. 343. Philadelphia: J. B. Lippincott Co., 1902.

THERE is probably no department of medical knowledge in which doctors disagree so widely as in the science and art of infant feeding, and thus it is no cause for wonder that the student finds it a difficult subject to understand when every authoritative text-book presents more or less exclusively the personal views and favorite methods of its author rather than a broad, impartial discussion of the underlying principles. We know of no one book hitherto published that can be said to present the subject completely, if perhaps we except Marfan's voluminous *Traité de l'Allaitement*, which, however, barely outlines the principles of percentage feeding, but contains none of the later very important contributions of Rotch and his followers of the American school.

For these reasons the book before us is a most welcome résumé of the work of all those who have contributed in greater or less degree to the development of our present knowledge of the subject. The substance of the work, as stated in the preface, "has been gleaned from the periodical literature, monographs, and text-books of the past eight years (1894–1901), so that this treatise may justly claim to be an authoritative statement of the views of the leading pediatrists and scientists of Europe and America on the subject of artificial feeding at the present day," being presented largely as classified extracts of their writings. As might be expected in a work of this character, conflicting statements occur, but in each case these are given under the name and usually in the words of the authorities responsible for them, so that no confusion is likely to arise.

An epitome of the subjects previously discussed in abstract is given by the authors in Chapter XII.—"The Principles of Infant Feeding"—in which the methods advocated by various authorities are classified under the headings of (1) Whole Milk; (2) Moderate Dilutions (*i. e.*, High Proteids); (3) High Dilutions (*i. e.*, Low Proteids); (4) Top Milk Mixtures; (5) Whey Mixtures; and (6) Laboratory Milk. In Chapter XIII. the various methods of scientific home modification are reviewed at length, and all of the commonly employed formulæ are

explained. In Chapter XIV. the authors outline a set of practical rules for the guidance of mothers in preparing home-modifications, applicable to any method of feeding. The chapter concludes with the description of a "method for calculating milk percentages without formulæ," which is designed to appeal to the practitioner who abhors mathematics, though the method necessarily differs little from that previously in use, except that an arithmetical formula replaces the algebraical one.

The concluding chapter on Artificial Foods is rather disappointing, containing little more than a classified list of proprietary foods, according to Cantley, with short abstracts from various authorities, generally uncomplimentary to such preparations, and similar opinions on condensed milk and peptonized milk. It is to be regretted that the authors have not embraced this opportunity to discuss authoritatively the proprietary foods; for however strongly most of them may be condemned, on both theoretical and clinical grounds, as continued substitutes for fresh milk mixtures, some of them have a distinct value under certain conditions in which a fresh milk modification is not tolerated, or is, for the time, impossible. Such a discussion by writers whose experience in infant feeding has been as extensive as that of Drs. Judson and Gittings would be appreciated by physicians who are accustomed to mention proprietary foods with bated breaths, and to prescribe them with implied or expressed apology.

The volume terminates with a bibliographical list containing 261 references and an appendix giving various analyses and the usual recipes for broths and diluents.

This book must be accepted as a unique contribution to the literature of infant feeding, and will prove a valuable work of reference.

T. S. W.

HEALTH, SPEECH, AND SONG: A PRACTICAL GUIDE TO VOICE PRODUCTION. By JUTTA BELL-RANSKE. London: Swan, Sonnenschein & Co.; New York: E. P. Dutton & Co., 1902.

THIS little book, by a professional musician, possesses considerable interest and value for all students and teachers of vocal music, for whom it is intended more than for the physician. For those of the medical profession, however, who are engaged in a special study of laryngology its pages will repay perusal as an exposition of the views of an artist and teacher of high standing. The part of the book which deals with the technique of singing is accurate and interesting. Where the author trespasses upon the province of the physician, however, she lays herself open to considerable criticism, the anatomy and physiology which she presents being of the school text-book variety, and consequently presenting many remarkable statements and theories. Many of Madame Bell-Ranske's views and methods are sure to impress themselves upon the artistic public, and this little book possesses the great merit of being a frank exposition of the personal experience of one whose lifework has lain among the subjects which it considers.

F. R. P

TEXT-BOOK OF PHYSIOLOGICAL AND PATHOLOGICAL CHEMISTRY. By G. BUNGE, M.D., Professor of Physiological Chemistry at Bale. Second English edition, translated from the fourth German edition by FLORENCE A. STARLING, and edited by ERNEST H. STARLING, M.D., F.R.S., Professor of Physiology in University College, London. Philadelphia: P. Blakiston's Son & Co.

THE title of this book is a misnomer; true, it is a text-book of physiological and pathological chemistry, but it is much more beside. Whoever picks it up merely to gain information in regard to chemical data and experimental results will put it down dissatisfied. The volume is singularly free from that disconnected mass of detail that disgusts and wearies the beginner; it consists, moreover, of a series of connected lectures that in their entirety constitute a thoughtful disquisition on biological problems based on the latter-day revelations of bio-chemistry and bio-physics.

Bunge is a mathematician and a chemist by training and by education, by temperament a poet with a philosophical bent of intellect. The complex character of the man is reflected in the book he has written. His life has been spent in observation and in experiment—that is his work, and in dreams and speculation—that is his amusement; the reader of the book is invited to share in both. From the height of metaphysical speculation he carries the reader down to the prose-level of dry dissertation, from sentences weighty with philosophical meaning to flights of delicate poetic imagery.

A happy philosophy illumines the work. The phenomena of life cannot be explained by mechanical laws alone; biological problems can never be elucidated by the understanding of structure. The riddle will merely become more complex; nevertheless, we must endeavor to advance as far as possible by the help of chemistry and physics and the microscope, realizing all the while that the smallest cell exhibits all the mysteries of life, and that our present method of *its* investigation by mechanical methods have reached their limit, realizing, too, that all the laws we deduce from the phenomenal world must be ascribed to human conceit.

"We transfer to the objects of our sensory perceptions, to the organs, to the tissue elements, and to every minute cell something which we have acquired from our own consciousness." Biological problems must be approached from within—we must project the conceptions of our "inner consciousness" into the outside world, must start from what we know, the internal world, to explain what we do not know, the external world.

Bunge fully recognizes the difficulties of this physiological method of inquiry, the vagueness of our perceptions in this field, and the limits of our faculties—but his optimism rises supreme—we do not know, but coming generations will know—science has no impossible boundaries—the type will be ennobled, and "a race may dominate the globe as superior to ourselves in intellectual faculties as we are to the infusoria."

The author's chief aim is to awaken interest, to initiate the reader into the study of biological problems, and to acquaint him with the principal achievements of bio-chemical research as applied to the phenomena of normal and perverted function. This object has been attained in a masterful manner. The physician will find his medical

studies simplified by a perusal of this volume, and he will gain a more intimate and a more comprehensive insight into the revelations of the exact sciences that form the groundwork of medicine. A. C. C.

A PRACTICAL MANUAL OF INSANITY. FOR THE STUDENT AND GENERAL PRACTITIONER. By DANIEL R. BROWER, A.M., M.D., LL.D., Professor of Nervous and Mental Diseases in Rush Medical College, in Affiliation with the University of Chicago, and in the Post-Graduate Medical School, Chicago; and HENRY BANNISTER, A.M., M.D., formerly Senior Assistant Physician, Illinois Eastern Hospital for the Insane. Octavo, 426 pages, with a large number of full-page inserts. Philadelphia and London: W. B. Saunders & Co., 1902.

THE better medical schools have in recent years offered instruction in mental diseases to their students. This has led to the multiplication of text-books on insanity. The one under review is a safe guide for students. Almost every writer on insanity tries to do two impossible things—define it and invent a classification. The former cannot be done until we learn the processes of thought, nor the latter until we know the causes, not the occasions, and the morbid anatomy of mental disease. The things we call the causes of insanity are no more causes than is the lighted match the cause of the explosion of gunpowder. The real cause is inherent in the powder, the match is merely the occasion. The author's definition is no worse than those of other writers, and their classification just as good. The book is well and clearly written, and is purely clinical. There is an entire absence of metaphysics and theory. Students will find it useful. C. W. B.

ATLAS AND EPITOME OF OTOLOGY. By GUSTAV BRÜHL, M.D., of Berlin, with the collaboration of PROFESSOR DR. A. POLITZER, of Vienna. Authorized translation from the German. Edited by S. MACCUEN SMITH, M.D., Clinical Professor of Otology, Jefferson Medical College, Philadelphia; Otologist and Laryngologist to the Germantown Hospital, Philadelphia. With 244 colored plates on 39 lithographic plates, and 99 text illustrations. Philadelphia and London: W. B. Saunders & Co., 1902.

THIS little book, which is certainly the best of its kind yet published on otology, fills a useful place. It combines in a thoroughly practical manner accurate and beautiful plates and their explanatory notes, with a text unusually exhaustive for so small a volume. Many of the plates are veritable works of art, and taken as a whole they easily surpass any previous collection. The portrayal of growths and malformations of the auricle, and also of mastoid operations, is especially praiseworthy.

The text, with well-executed illustrations, is divided into four general divisions: (1) Anatomy, (2) Physiology, (3) Examination, and (4) Pathology and Treatment. The first division goes into the minute

anatomy of the ear sufficiently for the student to obtain a thorough working knowledge of the parts, the plates assisting most materially in elucidating the descriptions. The development and delicate structures of the internal ear are shown unusually well. The chapters devoted to Physiology and Examination are quite short, the latter, however, giving the modern methods of diagnosis in a very pleasing manner.

The subjects of Pathology and Treatment are, from the student's standpoint, especially well handled. The usual multitudinous and oftimes confusing references to various authorities and methods of treatment are here conspicuous by their absence. The author states clearly and concisely what a large experience has taught him, and outlines the treatments which he has found to be most efficient in his hands and in those of the best otologists of the world to-day. Mastoiditis, brain abscess, sinus thrombosis, and pyemia are well described, and the modern treatment of them given, while the accompanying plates show the pathological lesions and operative technique very clearly. Taken as a whole, the book is remarkably free from inaccuracies either of the plates or text, and well deserves a good reception. W. R.

ELEMENTS OF PHYSICAL CHEMISTRY. By HARRY C. JONES, Johns Hopkins University, Baltimore, Md. New York: The Macmillan Co., 1902.

ANY book from the pen of Harry C. Jones, of Johns Hopkins University is hailed by the scientific world as a welcome addition to our literature in modern chemistry.

This book of 565 pages is a particularly valuable contribution to the science of chemistry. The subject is dealt with from the physical standpoint, and the twin sciences of physics and chemistry are so closely related (often spoken of as the "twin sister sciences") that the title "Elements of Physical Chemistry" is particularly well chosen, for as modern knowledge of chemistry increases, physics and our understanding of its laws play a more and more important part in the proper understanding and interpretation of chemical phenomena.

The book is divided into ten chapters, which respectively deal with atoms and molecules, gases, liquids, solids, solutions, thermochemistry, electrochemistry, photochemistry, chemical dynamics and equilibrium, and the measurements of chemical activity. These interesting topics are dealt with in a most clear and logical manner, and the historical development of them is particularly dwelt upon.

This new science of physical chemistry has practically come into existence during the past fifteen years. But the foundations for this were laid many years ago by such men as Kopp, Bunsen, Gladstone, Regnault, and others, and this the author does not ignore, but emphasizes the great value of their work, which has been built upon so successfully by such modern workers as Lathar-Meyer, Nernst, and that most brilliant of thinkers of the present day, Van Hoff, one of the originators of the "ion" theory of solutions and of stereochemical or space relations of the atoms. E. A. C.

THE STUDY OF THE PULSE, ARTERIAL, VENOUS, AND HEPATIC, AND OF THE MOVEMENTS OF THE HEART. By JAMES MACKENZIE, M.D. (Edin.). New York: The Macmillan Co., 1902.

THIS work consists of a series of personal observations upon a large number of cases extending over many years. The conclusions, while of greater interest to the physiologist, should also prove of benefit to the practitioner. The text is profusely illustrated with original sphygmographic tracings, and is subdivided into chapters and again into numbered sub-headings, adding greatly to its value for reference. The author advances original theories which are, for the most part, logically supported by tracings from cases cited. As an instance, may be mentioned his division of irregular pulse into two groups: (A) the youthful type of irregularity, when the irregularity occurs through variation in the duration of the diastolic period of the cardiac cycle, and (B) the adult type of irregularity, when there is a variation in the duration of the systolic period as well as in the diastolic period of the cardiac cycle.

Particular attention is called to the value of venous and liver tracings, which heretofore have attracted but little attention from the diagnostician. While it is difficult in a short review to give an adequate idea of this most carefully prepared work, yet it may be said broadly that it would be a valuable addition to the library of one who would correctly interpret the various phenomena of the circulatory apparatus.

T. A. C.

PROGRESSIVE MEDICINE. VOL. II., JUNE, 1902. A Quarterly Digest of Advancement, Discoveries, and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia. Octavo, 440 pages, 28 illustrations. Philadelphia and New York: Lea Brothers & Co.

THE June issue of *Progressive Medicine* is particularly interesting. The first portion, which relates to Surgery of the Abdomen, presents abstracts of a number of instructive contributions to surgical literature with well-chosen comments upon them. The second portion deals with Gynecological literature; the third, with Diseases of the Blood and Ductless Glands, Hemorrhagic Diseases, and Metabolic Diseases, and the fourth portion with Ophthalmology.

Coley, Clark, Stengel, and Jackson are the contributors, and this fact alone would suffice to insure the value of the volume. To us this volume is one of the most interesting of the late issues of this important publication. The articles relating to the subjects under discussion have been well chosen and well abstracted. As usual the editors of the various sections have not confined themselves to merely abstracting the articles dealing with the subjects upon which they write, but they have elaborated them and illuminated the topics by their own views and observations. It is this feature of *Progressive Medicine* which pre-

eminently distinguishes it from the various year-books and compendiums of medical knowledge which pour in such a flood from the press at the present time.

The volume is copiously illustrated with handsome cuts. J. H. G.

A Reference Handbook of the Medical Sciences, Embracing the Entire Range of Scientific and Practical Medicine and Allied Science. By Various Writers. A new edition, completely revised and rewritten. Edited by Albert H. Buck, M.D. Vol. IV. New York: William Wood & Co., 1902.

The last volume of the new edition of this invaluable publication covers from Ergot to Infiltrations. Its encyclopædic character renders it difficult to write an analytical review, the immense number of articles making it impossible to review all of them. As of special importance, however, may be mentioned the article by Royal Whitman on Disabilities of the Foot and Congenital Dislocation of the Hip. The article on Fractures, by Edward L. Keyes, Jr., is exhaustive and presents the most recent views on the subject. Glanders is considered by W. T. Councilman. Goitre is ably treated of by Joseph H. Pratt. The article on Wounds of the Heart, by Dr. Roswell Park, is worthy of the high standing of its author. Several biological questions of great interest are discussed, namely, Heredity, by Adami, and Evolution, by Bigelow.

In reviews of the previous volumes of this revised edition of this encyclopædia reference has been made to the fact that all of the articles have not only been revised but practically rewritten, so that the views presented are in accord with the very latest advancement in medical science.

The present volume contains quite a number of excellent colored plates, and, like the others, it is profusely illustrated with excellent pictures. F. R. P.

Essentials of Obstetrics. By Charles Jewett, A.M., M.D., Sc.D. 12mo., pp. 386. New York and Philadelphia: Lea Brothers & Co., 1901.

This is the best epitome of obstetrics with which we are familiar. It is sufficiently illustrated to make clear its text. Its contents are well selected, and attention drawn to salient features by judicious paragraphing and heavy type. It can be recommended to students and practitioners, and to lecturers who need to review salient points of obstetrics in preparing their instruction. E. P. D.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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On Diabetogenic Leucomaines.—LÉPINE (*Berl. klin. Wochenschr.*, 1902, xxxix. 346), in a brief communication, reports certain recent observations which tend to show that the blood of normal animals contains leucomaines, which, dissolved in water and injected subcutaneously in very small quantities into guinea-pigs, result in a more or less durable glycosuria.

Lépine and Boulud have shown that if a guinea-pig of normal size receive hypodermically the alcoholic extract of 5 grammes of the blood of a normal dog which has been redissolved in water, a transient glycosuria results. The extract of the same quantity of blood, however, from a dog from which the pancreas has been removed results in a glycosuria of several days' duration. Lépine concludes: "These experiments are in favor of an idea which I expressed two years ago, namely: that the pancreas in a physiological condition acts, at least in part, by destroying toxic diabetogenic substances. The absence of function of the pancreas results in an accumulation of these substances. Such is one of the elements of certain cases of diabetes."

Cytodiagnosis of Pleural Effusions.—GULLAND (*Scottish Medical and Surgical Journal*, June, 1902, p. 490) has made a study of the type of cells present in the fluid in cases of acute serous pleurisy. He is able to confirm the findings of Widal and Ravaut in France and of Wolff in Germany.

He finds that in tuberculous serous pleurisies the lymphocyte is by far the preponderating cell, polymorphonuclears being present in very small numbers.

On the other hand, effusions due to the pneumococcus and streptococcus in the serous stage, and before the exudate has become purulent, show an entirely different picture. The effusions show at all stages a great preponderance of polymorphonuclears over lymphocytes.

In cases of hydrothorax due either to cardiac or renal disease the cells in the exudate are very few in number and are mainly endothelial cells.

Gulland does not attempt in any way to lessen the importance of bacteriological examinations in all cases of pleural effusions. He wishes to show what others have found: that a preponderance of lymphocytes in a serous exudate is almost positive proof of its tuberculous origin. This knowledge is important, because it can be obtained three to six weeks before positive or negative results can be secured from the inoculation of guinea-pigs with the exudate, and the proper climatic and hygienic treatment can be immediately instituted.

The Treatment of Exophthalmic Goitre with Antithyreoidin.—SCHULTS (*Münchener medicinische Wochenschrift*, 1902, xlix. 834) says: Bearing in mind the probability that the symptoms of Graves' disease depend upon the excessive secretion of the thyroid gland, it occurred to Ballet and Enriquez that favorable results might be obtained by the introduction into the organism of such patients of the blood serum of animals from which the thyroid had been removed. They conceived it possible that such serum might contain an excess of poisonous substances normally neutralized by the thyroid secretion; that by the administration of such substances the harmful action or the excessive product of the thyroid gland might be neutralized. The use of the blood of patients with myxœdema was suggested by Burghardt, while Lanz suggested the use of the milk of goats upon which thyreodectomy had been performed. Moebius has used with success a preparation made by Merck, from the serum of sheep from which the thyroid had been removed. The author, shortly after Merck's remarks before the Society of Mid-German Psychiatrists and Neurologists, met with a typical case of Graves' disease with characteristic manifestations and serious mental symptoms. This patient was treated with rest and anti-thyreoidin in doses of from 0.5 to 4.5 grammes (gr. vijss–lxvij) three times a day. Forty-nine days after the beginning of treatment the patient was discharged from the hospital almost entirely well. The mental symptoms and the tremor had entirely disappeared and the goitre diminished materially in size. No unpleasant results were noticed from the treatment. In the same journal, Goebel (*Münchener medicinische Wochenschrift*, 1902, xlix. 835) reports a case in which favorable results were apparently obtained by the use of milk from a thyreoidectomized goat.

Blood Cultures in Pneumonia.—COLE (*Johns Hopkins Hospital Bulletin*, June, 1902, p. 136) made blood cultures in thirty cases chosen at random out of a total of sixty-three cases of pneumonia admitted to the medical wards of the Johns Hopkins Hospital during the session of 1901–1902. The object was to determine how frequently the blood was invaded with pneumococci during the course of the disease. The technique adopted in making blood cultures in typhoid fever was also followed here—that is, 8 to 10 cm. of blood was withdrawn and well diluted with bouillon so as to destroy the antibactericidal action of the blood serum. Several Erlenmeyer flasks containing 150 c.c. of bouillon were used in each case. Pneumococci grew from the blood in nine of the thirty cases in which cultures were made, all of

which terminated fatally. Altogether thirteen of the thirty cases died. Cole thinks that the taking of cultures is mainly of a prognostic value, the cases with pneumococcus septicæmia being much more likely to terminate fatally. Most other observers have obtained positive results in about the same percentage of cases in which cultures were made. Within the last year, however, Prochaska has published a series of fifty cases, in all of which he obtained the pneumococcus in the blood cultures. Of the fifty cases twelve died. This writer claims that there is no relationship between the number of organisms and the severity of the attack, but Cole challenges this view.

Peripheral Venous Thrombosis in Pneumonia, with Report of Three Cases and a Review of those Previously Recorded.—STEINER (*Johns Hopkins Hospital Bulletin*, June, 1902, p. 130) reports three cases of venous thrombosis occurring in a total of 500 cases of pneumonia at the Johns Hopkins Hospital. In the first case the right popliteal was involved. The patient had two attacks of pneumonia while in the hospital. The thrombosis occurred twenty-eight days after the crisis of the first attack and six days after the termination of the second attack. In the second case thrombosis of the right saphenous vein occurred on the sixth day of the disease, and death occurred on the twelfth day. The third patient had a thrombosis of the right popliteal vein, appearing six days after the temperature had returned to normal. Only one of the three cases died.

From the fact that he was able to collect only thirty-eight previously recorded cases in the literature, Steiner concludes that the condition must be rare, and remarks that this is surprising, considering the fact that the blood in pneumonia is so rich in fibrin. Thrombosis of the veins must be considered a sequel rather than a complication, as a vast majority of the cases occur after the temperature returns to normal. In all the cases the veins of the lower extremities were involved, and, as in typhoid fever and other infectious diseases, the left femoral is involved oftener than the right. Of the forty-one cases, death occurred in nine and recovery in twenty-five cases, no definite information being given in seven.

An Early Symptom of Pleurisy with Effusion.—On careful examination of the thorax in nineteen cases of pleurisy with effusion, fourteen serous, five suppurative, PRZEWALSKI (*Centralbl. f. Chirurgie*, 1902, xxix. p. 377) has observed, without exception, "a narrowing of the intercostal spaces and a more marked resistance to pressure in the spaces of the affected side." The symptom was most easily observed in children. "The drawing together of the ribs upon that side of the thorax which contains the exudation is wholly characteristic, and appears to offer a certain analogy to the muscular contractures in the extremities (attitudes fixes des membres) which is to be observed in the course of arthritides." The reason that this constant and typical symptom of pleurisy has never as yet been recognized lies in the fact, probably, that the change in position of each individual rib is so very slight. The author believes that this symptom depends upon the action of the internal intercostal muscles, and that it is probably to be regarded as a reflex contraction in the sense of Henle and Hunter.

[The observations with regard to the narrowing of the intercostal spaces is interesting. The increased resistance is familiar to most clinicians who have the good sense to use their fingers rather than a pleximeter and hammer.—W. S. T.]

Malarial Cirrhosis of the Liver of Splenic Origin; Indications for Splenectomy.—CARDARELLI (*Rivista Critica di Clinica Medica*, 1902, iii. 175). As is well known, splenic tumor may be an important symptom of cirrhosis of the liver, the enlargement depending upon passive congestion resulting from portal obstruction. But the association of events may be different; the enlargement of the spleen and the cirrhosis may depend upon the contemporaneous action upon the liver and the spleen of the same morbific agent, and, indeed, in some instances the splenic affection may represent the primary process, the hepatic cirrhosis the secondary. The observations of Chauffard have proven the existence of hepatitis of splenic origin, while the course of events in Banti's disease is an excellent example of the deleterious influenceupon the liver of processes primarily manifesting themselves in the spleen.

It is easily conceivable that in the chronic splenic enlargement of malarial origin substances might arise which, passing by the natural course of the circulation to the liver, might exert a deleterious influence upon the latter organ. While the majority of instances of enlarged spleen of malarial origin yield more or less readily to antimalarial treatment, the author asserts that it is not infrequent in Italy to observe cases in which, despite all treatment, the spleen remains enlarged, and that in exactly such instances the subsequent development of an apparently secondary cirrhosis is not infrequently observed. In such cases as this Cardarelli believes that splenectomy may be of very great value. The indications for operation he states as follows:

1. When, after vigorous and protracted treatment of months' and sometimes even of years' duration, the general condition of the patient shows no improvement, his color, his weight, his strength gradually fail, the examination of the blood shows progressive diminution in the amount of hæmoglobin, while there is no leukæmia, nor are malarial parasites present in the blood.

2. When the splenic tumor has attained considerable volume so as to occupy all or a good part of the left half of the abdomen; when it presents a more or less increased consistency, or is of unequal firmness, or shows deformations upon its surface or in its border; when there are indications of perisplenitis; when there is ectopia, and when the tumor, with medicinal treatment, shows no reduction in size or a very slow and slight change.

3. When the clinician, studying diligently the condition of the patient and the possible manifestations of incipient hepatic affection, has no doubt of the harmful influence of the spleen on the liver.

The main contraindications are cachexia, a reduction in hæmoglobin to a point under 30 or 40 per cent., leukæmia or tendency toward hemorrhages. Extensive adhesions between the tumor mass and the abdominal wall would, of course, also be a contraindication. A moderate ascites and the suspicion of an incipient hepatic cirrhosis should not entirely contraindicate operation. Operation is directly indicated in cases of ectopia or twisted pedicle. Statistics of splenectomies for enlarged malarial spleens show relatively good results. The removal of the spleen itself exercises no deleterious effect upon

the organism. The author believes that chronic splenic enlargement of malarial origin is often followed by cirrhosis; that its possible dependence upon processes going on in the spleen, and the good results of the removal of the spleen in such cases, justify this operation in those instances where medical treatment is of little or no avail.

SURGERY.

UNDER THE CHARGE OF

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The Diagnosis and Operative Treatment of Prostatic Hypertrophy, with Remarks on the Complications before and after Operation.—GUITÉRAS (*Medical News*, New York, April 26, 1902) states that the principal symptoms indicating the presence of an enlarged prostate are frequency of urination, pain, and spasm, and it is for their relief that the surgeon is usually consulted.

Indications for Operation. If the kidneys be in very bad condition medically or surgically, and if they be not improved by treatment, an operation is contraindicated, as uræmia may follow, shortening life instead of prolonging it. If there be very little residual urine, and if the kidneys be in good condition, it may be well to try at first stretching the prostatic urethra, and washing out the bladder if cystitis be present; but if there be considerable obstruction, as shown by the amount of the residual urine, and if the kidneys be affected in a mild degree, it is better to perform an operation as soon as possible. It must be remembered that prostatic symptoms occur most frequently in the fall of the year, and that they may be relieved by appropriate local and general treatment.

Complications before Operation. Attacks of epididymitis, hæmaturia, and urethral fever are complications which urge a patient more than anything to resort to operative procedures. Stone in the bladder is a frequent complication of enlarged prostate, and should receive attention. If the prostate be large in a case of stone, it would perhaps be better to do a suprapubic lithotomy and a prostatectomy. If a Bottini prostatotomy be contemplated it may be better, however, to perform this operation first, and to take advantage of the increased size of the urethra thus secured for the manipulation of litholapaxy. One must not forget that stone in the bladder is a more frequent complication of enlarged prostate than it is thought to be, and that the reason why we do not find it oftener is because we do not like to introduce solid instruments into the bladder, fearing to wound the pros-

tatic urethra. Very often, in old men with slightly enlarged prostates, it is the stone, and not the prostate, that is the cause of the trouble.

If there be a stricture complicating hypertrophied prostate, the operation can be made to include both conditions at the same time. It is extremely rare, however, to find strictures in men of the prostatic age, and almost all cases of so-called stricture in old men are cases of prostatic impediment in the posterior urethra.

In regard to the condition of the kidney and bladder, it may be said that the bladder is the least important, because it makes no difference how badly involved it may be, it will be benefited by the use of internal antiseptics and by irrigations through the catheter. An involved bladder does not count so much against the operation as does kidney involvement. It is surprising to see how often the bladder can empty itself almost entirely after a prostate operation, even if it has been previously considered atonic and years have been passed in catheter life. Diseased kidneys, however, whether medically or surgically involved, are always contraindications to surgical interference upon the prostate, as in such cases a renal congestion, followed by uræmia and death, may take place. If, then, the kidneys be diseased and an operation be demanded, a prostatotomy should be performed as the operation of choice, inasmuch as statistics show that the danger from this operation is very much less than from prostatectomy.

Valvular disease of the heart and fatty heart are indications against operations on the prostate if the heart action be poor. In the first class of cases the operation may be borne if there be sufficient compensatory hypertrophy of the heart muscle; in the second class it is always exceedingly dangerous.

Choice of Operation. The indications which would determine a choice between prostatectomy and prostatotomy (Bottini's operation) are the age of the patient, the size of the gland, and the condition of the bladder and kidneys. It may be said in general that cases in which there are slightly diseased kidneys and prostates that do not feel large on rectal examination, although they cause considerable urethral impediment, are cases for prostatotomy. On the other hand, middle-aged men with large prostates, as felt through the rectum, with good kidneys and sound bladders, are subjects for prostatectomy.

Age is an important consideration, for the older the patient the more liable he is to die from shock and asthenia; therefore, in a very old man, if the prostate be of the right variety, a Bottini operation should be performed. Cases of men over ninety years of age have been reported as successfully operated upon by this method. Old age is, however, not an absolute contraindication to prostatectomy, as men over seventy-five years old, having good kidneys, non-infected urine, but very large prostates, have successfully undergone this operation.

Regarding the size and shape of the prostate as influencing the choice of operation, it may be said that cases in which the prostate feels very large by rectum are suitable for enucleation, while cases in which the prostate does not feel considerably enlarged on rectal touch, but which offer a distinct impediment to the introduction of instruments into the prostatic urethra, and in which there is consequently a considerable amount of residual urine,

are best suited for prostatotomy. In this class of cases are those that present the so-called "prostatic bar" which is so often spoken of in connection with the subject of prostatic hypertrophy.

Preparation of the Patient for Operation. If the kidneys and bladder be in good condition, and there is not much residual urine, but little time is required to prepare the patient for operation. If the patient have acute retention of urine he should be handled with great care, and no more than sixteen ounces of urine should be drawn off at the first catheterization. After a lapse of four or five hours twelve more ounces should be drawn off, and then finally eight ounces should be drawn off every two hours until the bladder is empty. In all cases of retention the catheter should be introduced as often as indicated by the amount of urine passed and the frequency of the desire to urinate. In cases of acute retention after the bladder has been emptied the catheter should be used at first once every four hours; then, after the bladder is more tolerant, every five hours; later every six hours. If cystitis be present the bladder should be washed out twice a day with boric-acid solution, and once every day with a solution of silver nitrate 1 part in 4000. In addition some urinary antiseptic should be given. Under such treatment the amount of residual urine will begin to decrease, and more urine will be passed spontaneously. The catheter may then be used with diminishing frequency. It may be said, as a rule, that no patient with a marked degree of retention should be operated upon until he has been broken into "catheter life."

If the kidneys be affected with nephritis they must be brought into as good a condition as possible by appropriate medical treatment. If the kidneys be surgically involved, as, for example, in pyelonephritis, they may be kept flushed out with large quantities of water, and the diuretics mentioned, as well as such urinary antiseptics as urotropin, salol, sodium benzoate, and others will find a place in the treatment of such cases. The bowels should be moved and the rectum and bladder well washed out just before the operation is commenced. It is unnecessary to consider in detail the technique, possible complications during and after the Bottini operation, as they are now very well known. The results of this operation are most favorable, as a recent summary of the literature gives the statistics of 753 cases. In 622 of these the operation was successful, and only 44 deaths, or 5.8 per cent., are recorded. The technique and the complications of prostatectomy are also well known and require no detailed mention, but it is of interest to consider the results of this operation and to compare them with the Bottini method.

In the literature of the last few years there have been reported 152 cases of prostatectomy by the suprapubic, peritoneal, and the combined methods. Of these 95 were suprapubic operations, and the remainder perineal or combined. Among these cases there were 25 deaths and 127 recoveries. Of the latter class of cases 17 are spoken of as failures, 27 as successes, and the remainder as good results, improved, or recovered. It is difficult to say, therefore, what the exact results were in the cases spoken of as recoveries, excepting in the cases spoken of as failures and in those recorded as cured or successfully operated upon. Recovery, it must be remembered, may mean that the patient has either recovered from the operation or recovered his former health.

In comparing the results of these statistics on prostatectomy with those of prostatotomy, it will be noted that in prostatotomy 86 per cent. of the cases were cured, 5.8 per cent. died, and in 11 per cent. failures resulted; while in prostatectomy 78 per cent. of the cases were cured or improved, 16.5 per cent. died, and in 3 per cent. failure resulted. It will be seen, therefore, that the mortality in prostatectomy is three times greater than that of prostatotomy. In those who survive prostatectomy the failures are not as frequent as in those operated by the Bottini method. It is difficult to say, in fact, what constitutes a cure in these Bottini cases. It seems to me that if a patient can empty his bladder of all urine, excepting perhaps half an ounce of residuum, the result obtained can be said to be very satisfactory, especially if the patient be relieved of all his symptoms. Of course, the surgeon and the patient look upon the result from different view points. If the amount of residual urine be very materially decreased, and if the condition of the urine be improved, the surgeon considers the result satisfactory. On the other hand, the patient does not consider the result to be good unless the disagreeable symptoms, such as the frequency of urination, pain, tenesmus, and burning be removed. It may be said that in those who recover from prostatectomy the results are much better and more permanent than in patients successfully operated on by the Bottini method. In prostatectomy we never have to perform the operation but once, while prostatotomy may have to be repeated.

Conclusions. To sum up the clinical and statistical data obtained upon the subject of prostatic operations during the last few years, we must conclude:

1. That the general practitioner should be educated to palpate the prostate and to use the other simple means of diagnosis employed in determining the shape and size of the organ. In default of previous training in rectal palpation, he should at every opportunity familiarize himself with the feel of a normal prostate, and should thus educate his touch for prostatic diagnosis.

2. That the prostate corresponds pathologically in the male to the uterus in the female, and that its examination is just as important as uterine palpation, in which the general practitioner is, as a rule, far more expert.

3. That in prostatics the care of the bladder before operation is a prime factor. The importance of training such persons to observe the minutiæ of catheter life, of making the kidneys as active as possible, and of rendering the urine as nearly normal as possible before prostatic operations, cannot be over-estimated.

4. That every prostatic operation should be preceded by a thorough general examination, including an examination of the heart, the arteries, the urine, the bladder (for possible presence of stone or tumor) and of the urethra (for possible presence of a stricture), as well as by palpation of the kidneys.

5. That the statistics of the results of prostatic operations demonstrate that the successful cases belong most frequently to the class having a small amount of residual urine and a moderate prostatic enlargement. An early diagnosis is, therefore, of paramount importance.

6. That the choice of the operation must be based upon the lines drawn here, according to the age, the resisting power of the patient, and the size and shape of the prostate, with special reference to the seat and extent of the hypertrophy, as well as the condition of the kidneys and bladder.

7. That in the conduct of prostatotomy as well as prostatectomy, the prime object is to avoid so far as possible the occurrence of shock and to prevent the congestion of the kidneys by proper precautions during and by proper treatment after the operation.

THERAPEUTICS.

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The Transplantation of the Adrenals.—DR. V. SCHMIEDEN, in spite of the limitations to which investigations in this field are subject, particularly in the field of the transplantation of parenchymatous organs, has succeeded in transplanting portions of the adrenal glands of dogs to various parts of the same animal experimented on. Of great interest is the possibility of transplanting tissues in warm-blooded animals from one part of the body to another. The work of Strehl and Weiss, undertaken with reference to preventing death in animals deprived of their suprarenal capsules by means of portions of suprarenal gland transplanted to other localities, had not succeeded. These investigators sewed both organs in their entirety to the abdominal parietes, sometimes placed them free in the peritoneal cavity, in both cases without success. The same result attended the transplantation of slices of the adrenals. The author states that he has operated with various modifications upon dogs, and transplanted the adrenals as quickly as possible after extirpation. In no case was the entire gland removed, but always slices as large as one-fourth of the organ were transplanted. While small portions placed in the kidney became united to this organ without delay, and were found after six months unchanged both in their macroscopic and microscopic appearance, the author found that in the case of larger portions, particularly when placed in the peritoneal cavity, there resulted a central necrosis, although the peripheral zone remained alive. These results corresponded in every way with those obtained by von Eiselberg and Enderlen in the transplantation of pieces of the thyroid gland. The fact that certain transplanted portions of the adrenals failed to unite with the surrounding tissues, the author attributes largely to faulty technique. He proposes to repeat these experiments and also to try to graft portions of suprarenal gland from one animal to another, which he has not yet succeeded in doing.—*Archiv für die gesammte Physiologie*, 1902, vol. ix. p. 113.

The History of Uric Acid Introduced into the Organism.—DRS. F. SOETBEER and J. IBRAHIM experimented to determine whether circulating

uric acid is eliminated as such or is transformed into urea. Of eminent value in all future studies on the pathogenesis of the uric-acid diathesis and gout is the determination of the effect of the administration of uric acid either by mouth or subcutaneously. It has been generally accepted by physiological chemists that this substance, when artificially administered, disappears as such in the system and reappears in the urine under the form of urea. Some observers have found an increased output of uric acid following its introduction into the alimentary canal, attributing this either to the direct elimination of the unchanged acid, or at least to an indirect increase caused by the leucocytosis following the administration of this agent. In the case of uric acid introduced by the mouth, the experimenters found that the greater part of it is not absorbed in the alimentary canal; that its presence here causes no changes in metabolism, neither an increased nitrogen elimination nor an augmented production of uric acid. They reached the conclusion that the history of uric acid in the organism cannot be studied by watching the effects of its ingestion by the mouth, but that it is necessary to study the effects wrought by the subcutaneous administration of this agent. One of the authors was the subject of the research. After twenty-one days of careful feeding, so as to bring him into nitrogenous equilibrium, a solution containing a mixture of piperazin and uric acid was injected into the cellular tissue of the abdomen. Analysis of the urine showed on the day of the experiment a considerable increase of uric acid, the excess representing 80 per cent. of the uric acid administered. On the following day, when no uric acid was administered, the surplus of this substance in the urine continued, there being eliminated a little over 18 per cent. of the drug previously administered. The excess of uric acid on these two days represented practically all of this substance that had been injected. This was, however, not the only result, for on the three succeeding days there was a continuance of the surplus of uric acid in the urine. This latter fact showed that pathological changes occurred in the organism, which manifested themselves in causing a nitrogenous elimination amounting to 45 grains above the normal. Fever did not accompany this manifestation. The authors draw the following conclusions from their observations: (1) Circulating uric acid is eliminated as such, and not as urea; (2) it seems to act as a poison to the tissues, causing an increased production and consequent elimination of uric acid. Whether or not increased leucocytosis occurs in the course of these changes, the authors have not determined. They conclude that their researches afford a new perspective of those diseases accompanied by an increased uric-acid content of the blood, this increase causing by its toxic effects on the tissues a still greater production of uric acid, a "*circulus vitiosus*" being created. The original increase of this substance may be due to resistance to its elimination, as in nephritis or certain other unknown factors may come into play, as in gout.—*Zeitschrift für physiologische Chemie*, 1902, vol. xxxv. p. 1.

Bufonin and Bufotalin.—Dr. E. S. Faust has thoroughly studied the pharmacological action of the active ingredients of the secretion from the skin of lizards—bufonin and bufotalin. The latter closely resembles the drugs of the digitalin group, in that it increases the blood pressure, owing to

a rise of the pulse-volume and more forcible systolic contraction of the heart. The nervous apparatus of the heart is not influenced by it. After large doses cardiac paralysis with intact sensorium takes place. There is no direct action on the skeletal muscles and no local reaction on injection, as it is rapidly absorbed. Gastric disturbances are very common after both oral and hypodermic administration. The lethal dose is ½ milligramme per kilogramme. Bufonin, in the main, has the same action, but is much weaker, as less soluble; if, however, it be dissolved in dilute alcohol and injected, it may produce systolic arrest of the heart. Chemically, bufotalin differs from the drugs of the digitalis group, in that it is a weak acid.—*Archiv für experimentelle Pathologie und Pharmakologie*, 1902, vol. xlvii.

Action of Demulcents.—Dr. H. J. Tappeiner conducted a large number of experiments on animals and human beings to determine whether the group of drugs known as demulcents really possess the property of allaying irritation. A distinct diminished irritability of motor nerves by chemical salts was found in the presence of mucilaginous substances. The same can also be said of sensory nerves, since pain appeared later and was less intense than in control experiments. The mucous membranes of the eyes and of the intestines gave less evidence of inflammation when demulcents were added. On the other hand, the cathartic action of drugs is enhanced since their irritation is prolonged, owing to slowed absorption. It was also found that this absorption is less active in the stomach and the upper part of the intestines, and that this holds true for water alone. All these experiments prove that the time-honored custom of using the demulcent to allay inflammation and irritation is based upon scientific facts.—*Archives Internationales de Pharmacodynamique et de Therapie*, 1902, vol. x. p. 67.

The Bile and Saponification.—Dr. E. Pflüger discusses the conditions under which saponification occurs and the determination of the relative quantities of fatty acids and of soaps found in biliary mixtures. As ordinarily stated in the text-books, the formation of soaps in the small intestine is brought about by the union of the alkalies of the bile with the fatty acids produced by the splitting up of the fats. In a series of experiments the author has shown that bile in the presence of sodium carbonate and at the body temperature is able to bring about the solution of a considerable quantity of fatty acids. This solution cannot be accomplished without the presence of bile. His researches seemed to indicate that the solutions contained, beside soaps, considerable quantities of fatty acids in a free form. A general review of his last researches indicated that of the fatty acids dissolved in bile mixtures, only the smaller portion, at most 45 per cent., is dissolved through saponification. The author claims to have established the following conclusion, namely, that, strictly speaking, no freely dissolved fatty acids occur in bile mixtures, but that the former are present in a loosely combined state. It is remarkable, from both the physiological and the chemical standpoint, that the fatty acids form soluble acid salts, although there is present in the bile enough alkali to form neutral salts. The reason for this is the fact that the carbon dioxide contained in the sodium carbonate of the bile has a greater affinity for the sodium than have the fatty acids,

the neutral salts of which bind more readily a second molecule of fatty acid, although in a loose form. These significant facts make one understand why the transformation of the fatty acids into a soluble form requires one-half as much alkali as has been deemed necessary. The newer researches of the author show that the quantity of saponified fatty acids surpasses that of the freely dissolved fatty acids. Accordingly the provision has been made for the complete binding of all fatty acids by means of the neutral soaps, which are thus transformed into acid salts. The secret of the physiological significance of the bile in promoting the absorption of fats is to be found in the fact that the cholates dissolve the fatty acids, holding them in loose combination, and thus enable them to react with the sodium carbonate and the already formed neutral soaps. The cholates themselves undergoing no decomposition, a small portion of them have the power to bring about the transportation of a large quantity of fatty acids into neutral and acid salts. He showed by his investigations that the greatest quantity of fats that can at any time be absorbed can by means of the bile be made soluble in water. Since the action of the bile consists in the formation of neutral and acid soaps, the soluble form of the fats is the first to be taken into account from the standpoint of absorption. The latter can be accomplished without the intervention of bile; but, since the bile increases to a greater degree, the solubility of soaps, its presence in the jejunum and ileum augments the absorption of the soaps that occur there. It is probably in the epithelial cells that the soaps are retransformed into fatty acids and alkali, the former becoming neutral fat and the latter being taken up by the bloodvessels as sodium carbonate. Thus to the blood is restored the alkali that it has delivered into the intestine for the purposes of saponification. The discovery by Pawlow that the stimulation of the intestinal mucous membrane with acids causes an abundant flow of alkaline pancreatic juice furnishes a wonderful example of the self-regulating mechanism serving the needs of saponification. Moreover, fat itself is a powerful stimulus of the intestinal mucosa, whereby larger quantities of pancreatic juice, rich in steapsin, are secreted; and it is the opinion of Pawlow that fat exercises this power even in a neutral medium. This same investigator seeks the significance of this intimate relationship between acid stimulation and the pancreatic flow, in the fact that the alkali of the pancreatic juice inhibits the action of pepsin, favors the splitting action of the pancreatic enzymes, and restores the normal alkalescence of the blood. According to Pflüger, the excess of acids in the intestine produces a deficiency in the alkalies and consequently inhibits saponification, which, according to the author's law of self-regulation, excites the flow of richly alkaline pancreatic juice.—*Pflüger's Archiv für die gesammte Physiologie*, 1902, vol. xc. p. 1.

Respiratory Action of Some Drugs.—Drs. H. Hayashi and K. Muto have been studying some drugs which are known to affect the respiratory apparatus. They found that with curarine the conductivity of the peripheral ends of the motor nerves are diminished. Irritation of the nerve trunks by the secondary coil will still reach the muscle at first, but later, when the cerebral impulse is no longer active, all electricity is ineffective. With fungus poison arrest of respiration takes place owing to paralysis of

the phrenic; in large amounts an action similar to that of curarine occurs. Lastly, andromedotoxin was found to affect the motor nerves in such a way that, although they react normally to the electrical and the will impulse, they quickly are paralyzed after a short, strong irritation, but this paralysis disappears after a short rest. Respiratory disturbances are, however, due to centric causes in non-fatal doses; with fatal ones there is exhaustion of the respiratory centre.—*Archiv für experimentelle Pathologie und Pharmakologie*, 1902, vol. xlvii. p. 209.

Treatment of Sciatica.—DR. THIELLEMENT presents a parallel series of observations on the value of extradural injections of physiological salt solution and of cocaine in the treatment of sciatica, to the former of which the preference is given. In the injections of cocaine, anæsthesia is not produced in every case; pain usually disappears for from two to three days. The action of salt solution has given apparently similar results which were more lasting.—*Thèse de Paris*, 1001, No. 633.

GYNECOLOGY.

UNDER THE CHARGE OF

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Retroperitoneal Hæmatoma.—WALDSTEIN (*Centralblatt für Gynäkologie*, No. 24, 1902) reports the case of a nullipara, aged twenty-seven years, who had menstruated normally since the age of fifteen. Two years before she had a blow in the abdomen, followed by faintness and anæmia, and the appearance of a tumor the size of an orange. Frequent attacks of peritonitis followed, with a gradual increase in the swelling. On admission to the hospital she presented a fluctuating tumor as large as a man's head, occupying the left side of the abdomen and filling the pelvic inlet. Tympanitic resonance was noted over the tumor. The diagnosis of ovarian cyst with twisted pedicle was made, but on opening the abdomen the enlargement was found to be retroperitoneal and to have no connection with the pelvic organs, but was recognized as an hæmatocele of perirenal origin. Drainage was established after removal of the mass and the patient made a good recovery.

Arterio-Sclerosis as a Cause of Metrorrhagia.—GRUBE (*Centralblatt für Gynäkologie*, No. 25, 1902) describes the microscopic appearances of two uteri removed for obstinate hemorrhage. He found an excessive development of the connective tissue in the walls of the uterus, as well as in their

immediate neighborhood, and infers that the blood escaped per rhexin. He was unable to find any evidence of rupture of capillary walls, although old and recent collections of blood were often found throughout the uterine tissue. The diagnosis of this condition can be made only by exclusion. The material removed by curettement gives no clew to it. The writer holds that vaginal hysterectomy is clearly indicated in cases which resist all milder methods of treatment, atmokausis being uncertain in its results.

Abdominal Hysterectomy for Cancer.—DÖDERLEIN (*Centralblatt für Gynäkologie*, No. 26, 1902) begins a clinical lecture on the radical operation with the statement that five years should be allowed to elapse before a case is reported as cured. He cites the statistics of the Tübingen clinic for five years, in which 141 cases of total extirpation are recorded, with a mortality of 16 per cent.; 38 per cent. remained free from recurrence, 15 per cent. after the lapse of three years.

The writer speaks highly of Wertheimer's method of radical abdominal extirpation, and reports twenty-six cases operated upon by him since January of the present year, twenty patients surviving. He regards necrosis of the ureters as a real danger when they are denuded to a considerable extent. As regards the removal of glands, he notes that this was done in eighteen cases, cancerous infiltration being certainly observed in seven. Hardness of a gland, he believes, aside from increase in size, is a reliable criterion of infection. One must always fear that impalpable foci of disease in the lymph vessels and node have been overlooked. Probably in only one-third of the cases can infected glands be recognized and removed, which are always so situated that they could not be reached per vaginam. The writer concludes that this difficult and dangerous operation offers too little prospect of a radical cure to justify resort to it simply to prolong life.

Oil Enemata.—PUSINELLI (*Medizinische Wochen.*, No. 45, 1901) uses a quart of sweet oil in a three-necked flask, with one neck of which a vessel of water is connected, the pressure of which forces out the oil. The following indications for this treatment are recognized: Chronic constipation, especially when occurring in connection with membranous enteritis. In cases of neoplasm of the large intestine, especially cancer, accompanied by colicky pains and the passage of blood and mucus, oil injections give great relief where the question of operative intervention cannot be entertained. In recurrent appendicitis the writer finds this treatment excellent; also in the first stage in acute cases to relieve painful peristalsis and to clear the intestines of fecal masses. Obstinate constipation in women, accompanying enteroptosis, yields better to oil injections than to laxatives.

Treatment of Congenital Anteflexion.—ALEXANDROFF (*Frauenarzt*, Heft 193) describes the following operation for the relief of dysmenorrhœa due to congenital anteflexion: The os externum is drawn apart with two pairs of bullet-forceps, while an incision is carried downward along the anterior vaginal wall, beginning at the portio. The cervix is dissected off as in vaginal hysterectomy as high as the os internum, is then split, and each half is sutured to the edge of the vaginal wound on either side, in such a

way that the cervical endometrium is united to the submucous muscular layer of the vagina. The flaps of mucous membrane are next allowed to slide over the sutured edges, to which they are also sewn, thus covering all raw surfaces. A strip of iodoform gauze is introduced into the canal and the vagina is tamponed. The stitches are removed on the tenth day and the patient may leave her bed two days later.

Transplantation of Ovaries.—ROXAS and LUKASIEWICZ (*Frauenarzt*, Heft 194) found experimentally that ovaries can be transplanted from one animal to another, not only of the same, but of different species, and thus the after-effects of castration (non-oxidation of fats and hydrocarbons) can be prevented. The transplanted ovaries usually grow and retain their functions, though in some cases they atrophy within the first three months after operation, from insufficient vascular supply. The usual climacteric atrophy of the genitals and increase in adipose do not appear until later. The writer adds certain cautions with regard to technique. Strict asepsis must be maintained. The transplanted ovary must be carefully sutured to the mesovarium, as nearly as possible in its normal position, its lower half being covered with peritoneum. No stitches should be passed through ovarian tissue. Care must be taken that no pressure is made upon the ovary by neighboring organs.

Etiology of Hydrosalpinx.—MEEDERNOORT (*Revue de Gyn. et de Chir. Abdom.*, No. 4, 1901) discusses the question whether hydrosalpinx can develop without a previous catarrhal inflammation of the tube. Since the tube normally contains a small quantity of serous fluid, which is increased during menstruation, it follows that the hyperæmia of the tubal mucosa accompanying any abnormal condition of the uterus, especially fibromata, would naturally result in profuse secretion. This may also occur at the time of the climacteric.

Besides the accumulation of serous fluid in the tube, its distal end must be occluded. This may readily follow any mild degree of inflammation in the neighborhood, or even loss of the epithelial layer in consequence of extreme hyperæmia. A case is reported which developed at the menopause; careful microscopic investigation showed no evidence of inflammatory changes.

The Glands in Cancer of the Breast.—OZENNE (*Rêvue prat. d'Obstétrique et de Gynécologie*, 1901, No. 11) was able to keep twenty-three cases of cancer of the breast under observation from two to five years. In eleven cases the breast alone was removed, as the glands showed no evidence of being involved. In one instance, where the patient lived for ten years after operation, an enormous enlargement of one of the retropectoral glands was not disturbed, as it was regarded as purely inflammatory—in fact, it disappeared spontaneously.

Twelve patients from whom the axillary glands were removed at the same time with the breast had a recurrence within a year after operation. The writer refrained from removing the axillary glands in nine subsequent cases, with the result that two patients are now alive four years after operation, and five lived from two to three and a half years. The writer infers that

the results after these partial operations are quite as satisfactory as after the radical ones. While the principle of complete extirpation is theoretically ideal, he does not think that the results have shown that the hopes of a permanent cure have been realized. He is even inclined to believe that the extensive removal of glands may favor the spread of the disease to distant parts of the body.

OBSTETRICS.

UNDER THE CHARGE OF

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The Treatment of Puerperal Insanity.—JONES (*British Medical Journal*, 1902, Nos. 2149 and 2150) contributes a paper upon this subject, giving the results of his experiments in the London County Asylum.

Regarding the pathology of the condition, he calls attention to the changes of a toxæmic character occurring in the maternal blood. He believes the relation of general paralysis to this form of insanity to be accidental, for the paralysis had been in existence some time when pregnancy supervened. Insanity occurring after confinement must be referred, at least to some extent, to the absorption of waste material which should otherwise be discharged through the lochia. It is uncertain and improbable that all forms of puerperal insanity are due to the presence of bacterial poison. Some of the cases had no fever, the temperature remaining normal. Where septic infection cannot be diagnosed the cause must be considered as uræmic or due to some condition of the blood.

The pathology of lactation in insanity is practically that of insanity from exhaustion. The continued loss of albumin brings about a condition in which pneumonia with gangrene of the lung or phthisis may often supervene.

In selecting treatment it must be considered whether the case is that of pregnancy, childbirth, or the puerperal state. Out of fifty-six cases in which insanity occurred during pregnancy forty-seven went to full term. One died before confinement, the cause of death being given as vomiting, and autopsy revealing the lesions of general paralysis. Jones does not advise the induction of labor for insanity occurring during pregnancy, unless acute toxæmia or persistent nausea complicates the case. Patients usually recover from this condition, and the difficulties of maintaining asepsis make the induction of labor a dangerous thing. The violent outbreaks with fits of depression and fear, culminating in suicidal attempts, require the most constant vigilance on the part of attendants. Unless the patient can surround her-

self with the essential features of hospital care in her own home she should go to a hospital or an asylum. The general treatment includes a light dietary, gentle exercise, bright surroundings, the regulation of the bowels by saline aperients, and mild hypnotics to obtain sleep.

During the puerperal period insanity occurs in its most recoverable form, and well-to-do patients in the first attack should not be sent away from home within the first six weeks of the case. A strict watch must be kept upon the patient, and constant care is required to control the emotional disturbances and the tendency to infanticide and suicide.

In cases becoming chronic and stuporous good results have been seen from the use of the electric bath. The patient must be persistently fed often with the nasal tube during every quiet interval, as the exhaustion of active delirious mania in these cases is intense. Alcoholic stimulants are absolutely necessary. In 259 cases under review there was no proof that the cause of the affection was septic or of bacterial origin.

For feeding these cases eggs, beef-tea, milk, malt liquor, malt extract, and cod-liver oil were used, and, if required, free doses of calomel, podophyllin, jalap, or croton oil. In procuring sleep, opium and morphine should be avoided, and sulphonal, paraldehyde, and chloral and bromide should be selected. During the later stages of involution, iron, strychnine, and digitalis may be required. As anæmia disappears menstruation should return, which must be considered a most favorable sign.

Before recovery is complete, relapses with a return of mental confusion are sometimes seen after apparent convalescence. Sometimes a dull, listless condition is developed, which requires a special effort to overcome. In these cases a change should be made from a hospital to the patient's home, if possible. Vaginal douches of antiseptics hasten convalescence in some cases. Occasionally dilating and curetting the uterus are necessary, while hemorrhage is an uncommon complication. In two cases antistreptococcic serum was employed without result, and thyroid extract produced in some cases physical reaction, but no influence upon the mind. The breasts require special attention to prevent the formation of abscess. The excessive use of stimulants is not to be recommended during the puerperal state, and cases are sometimes seen which apparently owe their origin to this cause.

It must be remembered that the marriage of hysterical and neurotic persons should be strongly discouraged in the avoidance of insanity. The writer concludes by expressing his firm belief that insanity is the product of two factors—stress and heredity. The strain of pregnancy in a patient disposed to mental disease gives abundant opportunity for its development.

[The writer does not call attention to one danger which the reviewer has experienced in dealing with these cases. When the necessity arises for operation upon the parturient and insane patient the uterus reacts to all forms of interference very differently from that seen in normal patients. The induction of labor is most difficult, because the womb fails to contract under stimuli usually successful. During labor insane patients often become actively maniacal, and are controlled with the greatest difficulty. They may do great and even fatal injury to the child or to themselves at this time. The strange determination to destroy the child which is seen

in many cases renders the care of these patients difficult and makes constant vigilance imperative.]

Pelvic Changes in Symphysiotomy.—In the *Journal of Obstetrics and Gynecology of the British Empire*, March, 1902, SANDSTEIN contributes a paper upon this subject. He finds that after symphysiotomy three sorts of motions occur in the pelvis. The first is the movement of the pubes outward by rotation of the innominate bones on vertical axes passed through their respective iliac joints. This he considers of little importance. The second movement consists in rotation of the innominate bones on a horizontal transverse axis passing through the sacrum, and carries the pubes downward.

Besides these two movements a third and hitherto undescribed movement occurs. This consists in rotation of the innominate bone on its own axis so as to cause the ilium to become more erect or vertical. This movement of itself would cause shortening of the interspinous and intercristal diameters were it not more than compensated by the outward movement of the bones after pubic section.

The writer considers that Walcher is correct in maintaining that the pubes move downward to a considerable extent.

Regarding the increase in the various diameters of the pelvis, the conjugata vera was increased 1.67 millimetres per cm. of pubic separation. Roughly speaking, 6 cm. of pubic separation give 1 cm. of increase in the conjugata vera. The diagonal conjugate increased nearly two millimetres and the intertrochanteric over 6 millimetres, the intercristal 2.4 millimetres, and the interspinous 5.61 millimetres per centimetre of pubic separation. The transverse diameter of the brim increases 4 millimetres and the right and left oblique diameters of the brim 3.84 and 3.9 millimetres, respectively.

By comparing the gain in various diameters it is seen that the true significance of symphysiotomy during labor lies mainly in the fact that it permits increased descent of the pubic bones. Symphysiotomy is a means of obtaining greater effects than we can by Walcher's position. By Walcher's position the pubes can be depressed not more than 5 millimetres, whereas by symphysiotomy with 6 centimetres of pubic separation the mean depression of the pubes is 8.4 millimetres.

The danger of pubic separation lies in the damage done to the vulva, to the anterior vaginal wall, the urethra, and the bladder. Pubic separation should then be limited, if possible, to a maximum of 6 centimetres. Symphysiotomy, then, must be limited to cases in which by a gain of 1 centimetre, or two-fifths of an inch, in the true conjugate, the child may safely be delivered. The true conjugate must certainly not be below 7 centimetres, and should be above this measurement. The child must be living, and Walcher's position must be used, with support to the sides of the pelvis. Care must be taken to counteract unequal movements on the two sides of the pelvis. By flexing the thigh of the non-moving side and abducting the bent-up knee that side can be made to move equally with the other side, and the rupture of the ligaments avoided or delayed. The symphysis should be severed with a broad-bladed knife, and division of the

subpubic ligament should not be aimed at. This ligament prevents the extent of the wound down into the vulva. Ossification of the pubes does not occur, and hence the operator can always cut through cartilage. In 13.3 per cent. of cases the joint was in the median line, in 66.3 per cent. on the left side, and in 20 per cent. on the right. The tubercle upon the upper surface of the pubes is the best guide. Rigid asepsis is necessary, and infected cases should not be subjected to the operation.

OTOLOGY.

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Surgical Operations on the Middle Ear having for Their Object the Improvement of Hearing.—(Three articles by G. GRADINIGO, *Arch. f. Ohrenheilkunde*, Bd. liv., lv.). In the first article the author emphasizes three points of the subject to be considered:

1. The character of the middle-ear disease for which the operation is undertaken. All operative interference is contraindicated when the internal ear is also affected, as the reaction following the middle-ear operation causes an increase in the deafness depending on the inner-ear affection. Those cases of progressive deafness which are caused by lesions affecting chiefly the incus and malleus, the inner ear being intact—*i. e.*, ankylosis of or adhesions affecting these ossicles—are best adapted to surgical interference.

2. The method of operation. The conservative operations, such as simple perforation of the drum membrane, or removal of a segment of the same, or tenotomy of the tensor tendon, give only a temporary improvement. Gradinigo advises removal of the membrana tympani, malleus, incus, and, when possible, the stapes. This constitutes the "exenteratio cavi tympani." The removal of the stapes is only in certain cases practicable, as a high situation of the oval window and the delicacy of the arms of the ossicle lead often to fracture of the latter in the extraction, and the foot-plate remains behind. The removal of the incus alone, thus destroying the continuity of the abnormally fixed chain of ossicles, also accomplishes good results.

3. The post-operative treatment is of great importance. The reaction following the extraction of the ossicles, if of a severe type, influences unfavorably the final result for the hearing. Gradinigo has found that those cases of middle-ear adhesions which follow a catarrhal process, when operated are followed by less reaction than those which are consecutive upon a suppuration. The regeneration of the cicatricial membrana tympani should be

watched with great care, and granulations on the promontory which would lead to fixation with the new-formed membrana should be carefully avoided. After the formation of a new membrana its mobility should be ensured by suitable massage.

In the second article, Gradinigo describes the method of operation used by him, as follows: 1. Three small incisions through the drum membrane are made—one through the lower end of the vertical diameter of the membrane and one at either end of the horizontal diameter, all three being at and parallel to the border of the membrane. These three are then united by a circular incision, and the incision carried from either side to within a short distance of the neck of the malleus. The incision is not carried close to the neck of the malleus in order to avoid the vessels situated there. 2. Tenotomy of tensor tympani and division of any synechiæ. 3. Incision through the incudo-stapedial joint. 4. The incision around the border of the membrana, which was arrested a short distance from the hammer-neck in order to avoid an obscuring hemorrhage, is now finished up to the neck of the malleus on either side. The hammer is now extracted with the forceps of Faraci. 5. The incus is then extracted by grasping the long process with the forceps or it is swept down by a Zegroni hook if it is in the epitympanic space. 6. If the stapes is in sight it is either removed by means of pointed forceps after tenotomy of the stapedius, or it is mobilized.

Emphasis is placed on the post-operative treatment. The prevention of suppuration is of the first importance, and as a means to this end a gauze tampon which shall remain in place if possible thirty-six to forty-eight hours is advised. Syringing of the ear is contraindicated. The gauze tampon, after remaining thirty-six to forty-eight hours at first, should be renewed twice every twenty-four hours, but the tamponade should not be used longer than one week. The functional result of the exenteration of the cavum tympani, the author points out, depends on the nature of the disease process which causes the deafness, and he differentiates four classes: 1. Otosclerosis. 2. Chronic catarrhal inflammation. 3. Result of previous suppurative disease with intact membrana where the appearances are the same as in chronic catarrhal inflammation. 4. Results of previous suppurative disease where the membrana has been left perforated or wholly destroyed.

Class 1 (otosclerosis) can be distinguished by the thin, lustrous, movable drum membrane and often history of progressive deafness in the family.

Classes 2 and 3 present objectively the same picture, viz.: a thickened, lustreless, immovable, and often retracted drum membrane, and they can be distinguished from each other only by the history of the case.

Class 4 can be distinguished by simple inspection. As regards the functional examination, the author accepts the common differential signs—*i. e.*, shortened perception of the high tones in the sclerosis class, together with loss of the low tones, whereas in the other classes (2, 3, and 4) the chief defect is in the loss of the lower tones.

In the third and concluding article the author reports at considerable length the examination and results of operation in nine cases of progressive deafness. Two of these belonged to Class 1 (sclerosis). In neither of these was the stapes extracted, but it was mobilized in one. The improvement in hearing was considerable; in one case from inability to hear numerals in

conversation tone before operation above 0.25 m. distance to 1 to 1.5 m. after the lapse of one year after the operation. In Class 2 (chronic catarrhal middle-ear inflammation) three cases are reported. The stapes was not removed in any of these. The results were favorable in two of these cases. In Class 3 (chronic catarrhal, following suppurative, otitis) two cases are reported. In one (a double-sided affection) the stapes was removed from one side, and an attempt to remove it from the other was made, but the foot-plate remained in place. Marked improvement followed the operation. The second case was unsatisfactory, owing to labyrinthine involvement. Separate cases of Class 4 are not reported, but good results are claimed.

The reports of a case of chronic catarrhal otitis where the incus alone was removed, and one where the malleus was reduced from a retracted position to the normal position after tenotomy of the tensor tendon, show considerable improvement in the first case, but none in the second.

The author concludes as follows: The best results of exenteration of the cavum tympani are found in those cases following suppurative otitis where a destruction of the drum membrane has taken place (Class 4). Good results also follow in those cases (Class 3) where the diseased condition has resulted from previous suppurative disease without persistent perforation of the membrane or typical change in the same. In the first two classes (1 and 2—sclerosis and chronic catarrhal middle-ear inflammation) the operation was more successful in the sclerosis cases than in the catarrhal.

PATHOLOGY AND BACTERIOLOGY.

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The Intercommunicability of Human and Bovine Tuberculosis.—RAVENEL (*Proceedings of the Pathological Society of Philadelphia*, May, 1902, vol. v., No. 7) states that the probability of the transmission of tuberculosis from diseased cattle to man is a matter of such economic importance that, in lieu of definite proof in the matter, a greater or less attempt at eradication of this menace to public health by careful inspection of cattle has been going on for some years. Most men interested in the subject were somewhat startled by the emphatic propositions enunciated by Prof. Koch at the British Congress on Tuberculosis, last July, when he stated, first, that human tuberculosis differs from bovine, and cannot be transmitted to cattle; second, that the susceptibility of man to bovine tuberculosis is of

such rare occurrence, if it exists at all, that its import may be disregarded, and it is not advisable to take measures against it.

The first proposition is subject to direct experimental proof. Koch's statement was based on results obtained from nineteen attempts to infect healthy cattle by injecting tuberculous sputum into the jugular vein, peritoneal cavity, or subcutaneous tissues. On killing the animals after from six to eight months no traces of the disease were found in the internal organs. Controls with bovine tubercle bacilli were uniformly fatal.

After a carefully detailed review of successful experiments in producing tuberculosis in animals from human sputum conducted by Chauveau, Bollinger, Klebs, Crookshank, Martin, and others, Ravenel describes his own experiments along this line, conducted at the State Live-stock Sanitary Board during the last four years. With cultures of tubercle bacilli isolated both from human sputum and from the glands of generalized tuberculosis the author has been able to produce typical generalized tuberculosis in calves. He has further shown that successive passages through calves will increase markedly the virulence of such human cultures. He concludes from his own results and from those of others that Koch's first proposition is erroneous and untenable.

In judging the second and more important proposition we are naturally deprived of the conclusiveness of experimental data. The histological differences of human and bovine tuberculosis are more apparent than real, and the latest results show us that they are in no way essential to the problem. The morphological and cultural differences of human and bovine tubercle bacilli have been carefully studied by Theobald Smith and Ravenel. Morphologically, the bovine form is shorter and more uniform in size, and culturally it grows less readily; it is decidedly more pathogenic for laboratory animals than is the human form. Whether this criterion of pathogenicity holds for man must rest on a supposition in default of more direct evidence. The publication of Koch's paper has brought out many additional cases of transmission of tuberculosis from cattle to man. In addition to cases of generalized tuberculosis on rather definite evidence, many cases of localized occurrence of tuberculous lesions, principally verrucose tuberculosis of the skin, are reported. Koch bases his theory of the non-transmissibility of bovine tuberculosis chiefly on the alleged rarity of primary intestinal tuberculosis. The clinical observations on tuberculosis in children fed with tuberculous milk are not many, and are all open to criticism. From post-mortem examination it is difficult to prove that the point of entrance is through the intestine, and, on the other hand, we are far from justified in supposing that tuberculous lesions at points distant from the intestine may not owe their origin to this portal. Statistics as to the origin of the disease vary greatly in different countries both from actual differences and from the varying point of view of the observers. On the whole, the author feels assured that the greater part of the children who die of tuberculosis are infected through their food.

The number of cattle infected varies greatly in different regions, and many animals apparently free from disease have tuberculosis, and can give tuberculous milk from an udder that is in itself normal.

Strangely enough, Koch has not considered one very important means of

infection, namely, through the tonsils, many cases of which have been observed, and experimental reproduction of which in animals has been achieved.

In conclusion, we may assume from the evidence at hand "that human and bovine tuberculosis are but slightly different manifestations of the same disease, and that they are intercommunicable. Bovine tuberculosis is, therefore, a menace to public health.

"The eradication of bovine tuberculosis is amply justifiable from a purely economical standpoint; viewed in its bearing on human health it becomes a public duty."—F. P. G.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Insects and Human Diseases.—C. VON HOLUB (*Centralblatt für Bakteriologie*, etc., Band xxx., p. 284) makes the interesting communication that he has succeeded in infecting different species of insects with the streptobacillus of Ducrey, the cause of ulcus molle, in more than one thousand cases. Within several days after inoculation each insect became literally a package of pure culture of the organism. Every part of the organism—head, thorax, abdomen—was filled with the bacteria, and, although in the beginning there was in the pus of the ulcer a mixture of bacilli and cocci, in the insects there was nothing but pure cultures of the streptobacillus. Among the inoculated insects, those which were fed lived not longer than twenty-one days; those that were not fed lived only two weeks. Twelve hours after infection the development of the micro-organisms could already be observed.

The following proved to be susceptible to infection: Orthoptera, rhynchota, hemiptera, coleoptera, lepidoptera, diptera, and hymenoptera. Inoculation was performed by means of a very slender and sharp sterilized needle. The infected males conveyed the disease to members of the other sex, and in cages where numbers of insects were kept with only one that was inoculated all the rest became infected. Feeding with pus also caused infection.

The Significance of the Colon Bacillus in Drinking-water.—W. G. SAVAGE (*Journal of Hygiene*, July, 1902, p. 320), in an interesting article on the significance of the colon bacillus in drinking-water, quotes Jordan as objecting to that organism as a true index of sewage contamination, since it may be found in spring-water beyond any suspicion of contamination. Savage believes that it is not so much the presence of B. coli which is of positive value as the number present; that the kind of water in which this organism is found is of great importance; that a number of bacilli per litre of water from one source may be passed as safe, or at least as not evidence of danger of contamination, while the same number would be sufficient to

condemn water from another source; and that the exact point of the water-supply from which the sample is collected is of great importance. Frequently results differing considerably are obtained with samples taken from source and tap, respectively, and with arbitrary standards the one would be condemned and the other passed. His conclusions are as follows:

1. In estimating the significance of B. coli in a sample of water, the particular kind of water must be carefully considered; also the exact part of the system from which the sample was taken.

2. The number of B. coli present is an essential factor, but arbitrary standards of the number of this organism allowable per litre are of but little value, and are fraught with considerable possibilities of error unless the particular kind of water and the local conditions are considered in every case.

3. Waters which show no B. coli in 50 c.c. are of a high degree of purity, and, therefore, the proved absence of this organism in this amount, and, still better, in larger quantities, is of great value.

4. B. coli should be absent from at least 50 c.c. of spring-water; possibly from greater amounts.

5. In upland surface waters the presence of B. coli in 40, 10, or even 2 or 1 c.c. means contamination, but not necessarily a contamination which it is essential to prevent. It may be from contamination with the excreta of animals grazing on the gathering areas, and is by no means necessarily from sewage or other material containing specific organisms of infection. Further, there is no evidence that an amount of such animal contamination sufficient to cause a considerable number of B. coli per litre to be present in the water is harmful.

If B. coli are present in numbers greater than say 500 per litre (or even in that amount) such a water is suspicious, as it is rare to get so many B. coli in a water purely from the kind of animal contamination indicated, and further investigation is desirable. In filtered samples the number of B. coli is, as a rule, considerably reduced.

6. Chemical analysis cannot be considered a delicate method of detecting organic contamination, because it may fail with many waters in which pollution is undoubtedly taking place.

7. In surface wells, B. coli in large numbers indicate a surface or other contamination, generally very undesirable, if not actually dangerous. A knowledge of the position and the possibilities of contamination is very desirable in giving an opinion as to the purity of the water.

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